

=> file caplus

FILE 'CAPLUS' ENTERED AT 18:06:37 ON 01 MAY 2002

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Point of Contact:  
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CM1, Rm. 6B 01

FILE COVERS 1907 - 1 May 2002 VOL 136 ISS 18

FILE LAST UPDATED: 30 Apr 2002 (20020430/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D QUE L6

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON FORMOTEROL/CN  
L2 309 SEA FILE=CAPLUS ABB=ON PLU=ON L1  
L3 309 SEA FILE=CAPLUS ABB=ON PLU=ON 73573-87-2##/RN  
L4 309 SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR L3  
L5 273 SEA FILE=CAPLUS ABB=ON PLU=ON "DRUG DELIVERY SYSTEMS (L)  
AEROSOLS, INHALANTS"+OLD/CT  
L6 9 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND L5

=> D QUE L13

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON FORMOTEROL/CN  
L2 309 SEA FILE=CAPLUS ABB=ON PLU=ON L1  
L3 309 SEA FILE=CAPLUS ABB=ON PLU=ON 73573-87-2##/RN  
L4 309 SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR L3  
L9 1 SEA FILE=REGISTRY ABB=ON PLU=ON WATER/CN  
L10 246370 SEA FILE=CAPLUS ABB=ON PLU=ON L9  
L12 246370 SEA FILE=CAPLUS ABB=ON PLU=ON L9 OR L10  
L13 1 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND L12

=> D QUE L16

L14 405 SEA FILE=CAPLUS ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L15 2639836 SEA FILE=CAPLUS ABB=ON PLU=ON AQUEOUS OR WATER  
L16 0 SEA FILE=CAPLUS ABB=ON PLU=ON L14 (3A) L15

=> D QUE L17

L14 405 SEA FILE=CAPLUS ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L15 2639836 SEA FILE=CAPLUS ABB=ON PLU=ON AQUEOUS OR WATER

L17                    2 SEA FILE=CAPLUS ABB=ON   PLU=ON   L14 (5A) L15

=> S L6 OR L13 OR L17

L94                    11 L6 OR L13 OR L17

=> FILE MEDLINE

FILE 'MEDLINE' ENTERED AT 18:07:41 ON 01 MAY 2002

FILE LAST UPDATED: 1 MAY 2002 (20020501/UP).   FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded.   See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records.   See HELP CONTENT for details.

MEDLINE is now updated 4 times per week.   A new current-awareness alert frequency (EVERYUPDATE) is available.   See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary.   Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index.   See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> D QUE L33

L18	409	SEA FILE=MEDLINE ABB=ON	PLU=ON	FORMOTEROL OR AFORMOTEROL OR EFORMOTEROL OR FORMADIL
L19	336	SEA FILE=MEDLINE ABB=ON	PLU=ON	73573-87-2
L20	409	SEA FILE=MEDLINE ABB=ON	PLU=ON	L18 OR L19
L21	16146	SEA FILE=MEDLINE ABB=ON	PLU=ON	AEROSOLS/CT
L23	20	SEA FILE=MEDLINE ABB=ON	PLU=ON	L20 AND L21
L24	3909	SEA FILE=MEDLINE ABB=ON	PLU=ON	NEBULIZERS AND VAPORIZERS/CT
L33	4	SEA FILE=MEDLINE ABB=ON	PLU=ON	L23 AND L24

=> D QUE L35

L19	336	SEA FILE=MEDLINE ABB=ON	PLU=ON	73573-87-2
L30	41374	SEA FILE=MEDLINE ABB=ON	PLU=ON	7732-18-5##
L35	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	L19 AND L30

=> D QUE L40

L18	409	SEA FILE=MEDLINE ABB=ON	PLU=ON	FORMOTEROL OR AFORMOTEROL OR EFORMOTEROL OR FORMADIL
L19	336	SEA FILE=MEDLINE ABB=ON	PLU=ON	73573-87-2
L20	409	SEA FILE=MEDLINE ABB=ON	PLU=ON	L18 OR L19
L21	16146	SEA FILE=MEDLINE ABB=ON	PLU=ON	AEROSOLS/CT
L39	2590	SEA FILE=MEDLINE ABB=ON	PLU=ON	L21/MAJ
L40	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	L20 AND L39

=> D QUE L42

L18	409	SEA FILE=MEDLINE ABB=ON	PLU=ON	FORMOTEROL OR AFORMOTEROL OR EFORMOTEROL OR FORMADIL
-----	-----	-------------------------	--------	--

L19 336 SEA FILE=MEDLINE ABB=ON PLU=ON 73573-87-2  
L20 409 SEA FILE=MEDLINE ABB=ON PLU=ON L18 OR L19  
L22 11508 SEA FILE=MEDLINE ABB=ON PLU=ON ADMINISTRATION, INHALATION/CT  
  
L41 143 SEA FILE=MEDLINE ABB=ON PLU=ON L22/MAJ  
L42 0 SEA FILE=MEDLINE ABB=ON PLU=ON L41 AND L20

=> D QUE L44

L18 409 SEA FILE=MEDLINE ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L19 336 SEA FILE=MEDLINE ABB=ON PLU=ON 73573-87-2  
L20 409 SEA FILE=MEDLINE ABB=ON PLU=ON L18 OR L19  
L24 3909 SEA FILE=MEDLINE ABB=ON PLU=ON NEBULIZERS AND VAPORIZERS/CT  
L43 1971 SEA FILE=MEDLINE ABB=ON PLU=ON L24/MAJ  
L44 8 SEA FILE=MEDLINE ABB=ON PLU=ON L20 AND L43

=> D QUE L48

L45 409 SEA FILE=MEDLINE ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L46 282134 SEA FILE=MEDLINE ABB=ON PLU=ON AQUEOUS OR WATER  
L48 1 SEA FILE=MEDLINE ABB=ON PLU=ON L45 (5A) L46

=> S L33 OR L44 OR L48

L95 10 L33 OR L44 OR L48

=> FILE EMBASE

FILE 'EMBASE' ENTERED AT 18:09:13 ON 01 MAY 2002

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FILE COVERS 1974 TO 25 Apr 2002 (20020425/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> D QUE L54

L49 1043 SEA FILE=EMBASE ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L50 946 SEA FILE=EMBASE ABB=ON PLU=ON 73573-87-2  
L51 1043 SEA FILE=EMBASE ABB=ON PLU=ON L49 OR L50  
L52 246 SEA FILE=EMBASE ABB=ON PLU=ON L51 AND IH/CT  
L53 1656 SEA FILE=EMBASE ABB=ON PLU=ON NEBULIZATION/CT  
L54 5 SEA FILE=EMBASE ABB=ON PLU=ON L52 AND L53

=> D QUE L59

L49 1043 SEA FILE=EMBASE ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L50 946 SEA FILE=EMBASE ABB=ON PLU=ON 73573-87-2  
L51 1043 SEA FILE=EMBASE ABB=ON PLU=ON L49 OR L50  
L52 246 SEA FILE=EMBASE ABB=ON PLU=ON L51 AND IH/CT  
L53 1656 SEA FILE=EMBASE ABB=ON PLU=ON NEBULIZATION/CT  
L55 15781 SEA FILE=EMBASE ABB=ON PLU=ON AEROSOL/CT  
L57 19 SEA FILE=EMBASE ABB=ON PLU=ON L55 AND L52  
L59 2 SEA FILE=EMBASE ABB=ON PLU=ON L57 AND L53

=&gt; D QUE L63

L49 1043 SEA FILE=EMBASE ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L62 304738 SEA FILE=EMBASE ABB=ON PLU=ON WATER OR AQUEOUS  
L63 0 SEA FILE=EMBASE ABB=ON PLU=ON L49 (5A) L62

=&gt; D QUE L65

L53 1656 SEA FILE=EMBASE ABB=ON PLU=ON NEBULIZATION/CT  
L60 946 SEA FILE=EMBASE ABB=ON PLU=ON FORMOTEROL/CT  
L64 412 SEA FILE=EMBASE ABB=ON PLU=ON L60/MAJ  
L65 0 SEA FILE=EMBASE ABB=ON PLU=ON L64 AND L53

*Formoterol major focus  
of document.*

=&gt; D QUE L69

L55 15781 SEA FILE=EMBASE ABB=ON PLU=ON AEROSOL/CT  
L60 946 SEA FILE=EMBASE ABB=ON PLU=ON FORMOTEROL/CT  
L64 412 SEA FILE=EMBASE ABB=ON PLU=ON L60/MAJ  
L68 19 SEA FILE=EMBASE ABB=ON PLU=ON L64 AND L55  
L69 4 SEA FILE=EMBASE ABB=ON PLU=ON L68 AND IH/CT

*IH = Inhalation  
delivery*

=&gt; D QUE L72

L19 336 SEA FILE=MEDLINE ABB=ON PLU=ON 73573-87-2  
L71 24661 SEA FILE=EMBASE ABB=ON PLU=ON 7732-18-5##  
L72 1 SEA FILE=EMBASE ABB=ON PLU=ON L19 AND L71

=&gt; S L54 OR L59 OR L69 OR L72

L96 10 L54 OR L59 OR L69 OR L72

=&gt; FILE DRUGU

FILE 'DRUGU' ENTERED AT 18:10:31 ON 01 MAY 2002  
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FILE LAST UPDATED: 26 APR 2002 &lt;20020426/UP&gt;

&gt;&gt;&gt; DERWENT DRUG FILE (SUBSCRIBER) &lt;&lt;&lt;

&gt;&gt;&gt; SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001. &lt;&lt;&lt;

&gt;&gt;&gt; (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION &lt;&lt;&lt;

&gt;&gt;&gt; SEE HELP COST &lt;&lt;&lt;

&gt;&gt;&gt; FILE COVERS 1983 TO DATE &lt;&lt;&lt;

&gt;&gt;&gt; THESAURUS AVAILABLE IN /CT &lt;&lt;&lt;

=&gt; D QUE L81

L73 737 SEA FILE=DRUGU ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L81 0 SEA FILE=DRUGU ABB=ON PLU=ON L73 (3A) (AQUEOUS OR WATER)

=&gt; D QUE L82

L73 737 SEA FILE=DRUGU ABB=ON PLU=ON FORMOTEROL OR AFORMOTEROL OR  
EFORMOTEROL OR FORMADIL  
L82 1 SEA FILE=DRUGU ABB=ON PLU=ON L73 (5A) (AQUEOUS OR WATER)

=&gt; D QUE L83

L73            737 SEA FILE=DRUGU ABB=ON   PLU=ON   FORMOTEROL OR AFORMOTEROL OR  
                  EFORMOTEROL   OR FORMADIL  
 L74            457 SEA FILE=DRUGU ABB=ON   PLU=ON   73573-87-2  
 L75            737 SEA FILE=DRUGU ABB=ON   PLU=ON   L73 OR L74  
 L79            42824 SEA FILE=DRUGU ABB=ON   PLU=ON   WATER OR 7732-18-5  
 L80            12 SEA FILE=DRUGU ABB=ON   PLU=ON   L75 AND L79  
 L83            11 SEA FILE=DRUGU ABB=ON   PLU=ON   L80 AND 33/CC

*33 is "respiratory"  
 section code*

=> S L82 OR L83  
 L97            12 L82 OR L83

=> FILE WPIDS  
 FILE 'WPIDS' ENTERED AT 18:11:31 ON 01 MAY 2002  
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FILE LAST UPDATED: 29 APR 2002                    <20020429/UP>  
 MOST RECENT DERWENT UPDATE                    200227   <200227/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been  
 enabled in WPINDEX/WPIDS and WPIX >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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=> D QUE L87  
 L84            110 SEA FILE=WPIDS ABB=ON   PLU=ON   FORMOTEROL OR AFORMOTEROL OR  
                  EFORMOTEROL   OR FORMADIL  
 L85            1246207 SEA FILE=WPIDS ABB=ON   PLU=ON   WATER OR AQUEOUS  
 L87            1 SEA FILE=WPIDS ABB=ON   PLU=ON   L84 (5A) L85

=> D QUE L90  
 L84            110 SEA FILE=WPIDS ABB=ON   PLU=ON   FORMOTEROL OR AFORMOTEROL OR  
                  EFORMOTEROL   OR FORMADIL  
 L85            1246207 SEA FILE=WPIDS ABB=ON   PLU=ON   WATER OR AQUEOUS  
 L88            18208 SEA FILE=WPIDS ABB=ON   PLU=ON   AEROSOL?  
 L89            25 SEA FILE=WPIDS ABB=ON   PLU=ON   L84 AND L88  
 L90            7 SEA FILE=WPIDS ABB=ON   PLU=ON   L89 AND L85

=> D QUE L93  
 L84            110 SEA FILE=WPIDS ABB=ON   PLU=ON   FORMOTEROL OR AFORMOTEROL OR  
                  EFORMOTEROL   OR FORMADIL  
 L85            1246207 SEA FILE=WPIDS ABB=ON   PLU=ON   WATER OR AQUEOUS  
 L91            1121 SEA FILE=WPIDS ABB=ON   PLU=ON   NEBULIZ? OR NEBULIS?  
 L92            9 SEA FILE=WPIDS ABB=ON   PLU=ON   L84 AND L91  
 L93            7 SEA FILE=WPIDS ABB=ON   PLU=ON   L92 AND L85

=> S L87 OR L90 OR L93  
L98 9 L87 OR L90 OR L93

=> FILE STNGUIDE  
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Apr 26, 2002 (20020426/UP).

=> DUP REM L95 L97 L94 L96 L98  
FILE 'MEDLINE' ENTERED AT 18:14:41 ON 01 MAY 2002

FILE 'DRUGU' ENTERED AT 18:14:41 ON 01 MAY 2002  
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PROCESSING COMPLETED FOR L95  
PROCESSING COMPLETED FOR L97  
PROCESSING COMPLETED FOR L94  
PROCESSING COMPLETED FOR L96  
PROCESSING COMPLETED FOR L98  
L99 48 DUP REM L95 L97 L94 L96 L98 (4 DUPLICATES REMOVED)

=> D IBIB AB CT 1-48

L99 ANSWER 1 OF 48 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:122774 CAPLUS  
DOCUMENT NUMBER: 136:172782  
TITLE: Formulations of mometasone and a bronchodilator for  
pulmonary administration  
INVENTOR(S): Kaplan, Leonard W.; Weinrich, Karl P.; Iorio, Theodore  
L.  
PATENT ASSIGNEE(S): Longwood Pharmaceutical Research, Inc., USA  
SOURCE: PCT Int. Appl., 37 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011711	A2	20020214	WO 2001-US24093	20010801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,				

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY/APPLN. INFO.: US 2000-223541P P 20000804

AB A pharmaceutical formulation is provided for pulmonary drug administration of a bronchodilator, a corticosteroid and an optional pharmaceutically acceptable carrier. The bronchodilator has agonist activity for .beta.2-adrenergic receptors. In addn., methods for using the formulation to treat bronchodilator/corticosteroid-responsive conditions, diseases or disorders are provided, as are drug delivery devices and dosage forms for housing and/or dispensing the formulations. For example, pirbuterol acetate 10.0 mg, mometasone furoate 10.0 mg, and lactose 2000 mg were blended using conventional blending techniques to form a dry powder. Particle size redn. was not required as each of the components is obtained having a suitable particle size. The dry powder was then divided, in equal portions, into 100 capsules each contg. 100 .mu.g of pirbuterol acetate and 100 .mu.g of mometasone furoate.

CT **Drug delivery systems**  
 CT Drug delivery systems  
 CT Hydrocarbons, biological studies  
 CT Antiasthmatics  
 CT Bronchodilators  
 CT Lung, disease  
 CT Propellants (sprays and foams)  
 CT Corticosteroids, biological studies  
 CT Hydrocarbons, biological studies  
 CT Perfluorocarbons  
 CT Hydrocarbons, biological studies  
 CT Drug delivery systems  
 CT Medical goods  
 CT Drug delivery systems  
 CT Drug delivery systems  
 CT Drug delivery systems  
 CT Adrenoceptor agonists

L99 ANSWER 2 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:51237 CAPLUS

DOCUMENT NUMBER: 136:123631

TITLE: Aerosol formulation containing a polar fluorinated compound

INVENTOR(S): Rogueda, Philippe

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003958	A1	20020117	WO 2001-SE1606	20010710
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-16876 A 20000711

AB The present invention relates to a stable pharmaceutical aerosol formulation intended for inhalation. The formulation contains an active substance, an aerosol propellant, a polar fluorinated mol. and an excipient. The preferred propellant is HFA 134a or HFA 227 or a mixt. Thus, an aerosol formulation contained budesonide 0.125, methoxy-PEG-DSPE 0.320, 1H,1H,2H,2H-perfluorooctan-1-ol 31.7 and HFA-227 to 100%.

CT Polyoxyalkylenes, biological studies  
CT Allergy inhibitors  
CT Analgesics  
CT Anti-inflammatory agents  
CT Antiasthmatics  
CT Antibiotics  
CT Antihistamines  
CT Antitumor agents  
CT Bronchodilators  
CT Cardiovascular agents  
CT Cholinergic antagonists  
CT Imaging agents  
CT Leukotriene antagonists  
CT Lung  
CT Propellants (sprays and foams)  
CT Pulmonary surfactant  
CT Tuberculostatics  
CT Virus vectors  
CT Metals, uses  
CT Carbohydrates, biological studies  
CT Castor oil  
CT Enzymes, biological studies  
CT Fatty acids, biological studies  
CT Fluoropolymers, biological studies  
CT Peptides, biological studies  
CT Perfluoro compounds  
CT Perfluorocarbons  
CT Phospholipids, biological studies  
CT Polyoxyalkylenes, biological studies  
CT Polyoxyalkylenes, biological studies  
CT Proteins  
CT Steroids, biological studies  
CT **Drug delivery systems**  
CT Drug delivery systems  
CT Glycosides  
CT Polyoxyalkylenes, biological studies  
CT Lung, disease  
CT Fatty acids, biological studies  
CT Polyesters, biological studies  
CT Alkanes, biological studies  
CT Mast cell  
CT Drug delivery systems  
CT Polyoxyalkylenes, biological studies  
CT Polyesters, biological studies  
CT Nose

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 3 OF 48 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-164809 [21] WPIDS



DOC. NO. CPI: C2002-050997  
TITLE: Medicinal **aerosol** formulation used for  
pressurized drug delivery for treating e.g. asthma  
comprises particulate medicament, propellant and  
stabilizer comprising **water** addition.  
DERWENT CLASS: B05 B07  
INVENTOR(S): ADJEI, A L; CUTIE, A J  
PATENT ASSIGNEE(S): (AERO-N) AEROPHARM TECHNOLOGY INC  
COUNTRY COUNT: 93  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
-----					
WO 2002007672	A2	20020131	(200221)*	EN	18
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM					
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC					
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE					
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
-----			
WO 2002007672	A2	WO 2000-US42625	20001207

PRIORITY APPLN. INFO: US 2000-619183 20000719

AB WO 200207672 A UPAB: 20020403

NOVELTY - Medicinal **aerosol** formulation (I) comprises:(a) at particulate medicament or combination of at least two  
medicaments;

(b) propellant, and

(c) stabilizer comprising **water** addition in an amount which  
is in addition to nascent formulation **water**.DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the  
following:

(1) preparation of (I), and

(2) a metered dose inhaler containing (I).

ACTIVITY - Antiallergic; Antiinflammatory; Antidiabetic; Antianginal;  
Antibacterial.

MECHANISM OF ACTION - None given in the source material.

USE - Used for pressurized drug delivery to effect bronchodilation  
for treating asthma, chronic obstructive pulmonary disease, allergic  
rhinitis, rhinitis, diabetes, angina and local infection.ADVANTAGE - The stabilizer prevents settling, creaming or  
flocculation of (I).

Dwg.0/0

L99 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:146364 CAPLUS

TITLE: Electrochemical behavior of formoterol fumarate and  
its determination in capsules for inhalation and human  
serum using differential-pulse and square-wave  
voltammetry

AUTHOR(S): Demircigil, B. T.; Ozkan, S. A.; Coruh, O.; Yilmaz, S.

CORPORATE SOURCE: Faculty of Pharmacy, Department of Analytical  
Chemistry, Gazi University, Ankara, 06330, Turk.

SOURCE: Electroanalysis (2002), 14(2), 122-127

CODEN: ELANEU; ISSN: 1040-0397  
PUBLISHER: Wiley-VCH Verlag GmbH  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The electrochem. oxidn. of formoterol fumarate (**formoterol**) has been carried out in **aq. soln.** in the pH range of 1.5-10.0 by cyclic, linear sweep, differential-pulse and square-wave voltammetry. The diffusion controlled nature of the waves was established. The mechanism of oxidn. was discussed. Two voltammetric techniques for the detn. of formoterol in 0.5 M sulfuric acid which allow quantitation over the 8 .times. 10<sup>-6</sup>-6 .times. 10<sup>-5</sup> M range for both methods were proposed. Based on this study simple, rapid and selective two voltammetric methods were developed for the detn. of formoterol in capsule dosage form and human serum.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 5 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002079718 EMBASE

TITLE: [System of inhalation in asthma therapy].

LES SYSTEMES D'INHALATION DANS LE TRAITEMENT DE L'ASTHME.

AUTHOR: Dubus J.C.; Andrieu V.; Reynier J.P.

CORPORATE SOURCE: J.C. Dubus, Unite de Medecine Infantile, CHU  
Timone-Enfants, 13385 Marseille Cedex 5, France.  
jdubus@mail.ap-hm.fr

SOURCE: Revue des Maladies Respiratoires, (2002) 19/1 (90-92).

Refs: 5

ISSN: 0761-8425 CODEN: RMREEY

COUNTRY: France

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
027 Biophysics, Bioengineering and Medical  
Instrumentation  
037 Drug Literature Index

LANGUAGE: French

CT Medical Descriptors:

\*asthma: DT, drug therapy

**aerosol**

inhaler

**nebulization**

metered dose inhaler

human

article

Drug Descriptors:

salbutamol sulfate: DT, drug therapy

**salbutamol sulfate: IH, inhalational drug administration**

salbutamol: DT, drug therapy

**salbutamol: IH, inhalational drug administration**

fluticasone propionate: DT, drug therapy

**fluticasone propionate: IH, inhalational drug administration**

beclometasone dipropionate: DT, drug therapy

**beclometasone dipropionate: IH, inhalational drug administration**

pirbuterol acetate: DT, drug therapy

**pirbuterol acetate: IH, inhalational drug administration**

salmeterol xinafoate: DT, drug therapy

**salmeterol xinafoate: IH, inhalational drug administration**

fluticasone propionate plus salmeterol: DT, drug therapy

**fluticasone propionate plus salmeterol: IH, inhalational drug administration**

terbutaline: DT, drug therapy

terbutaline: IH, inhalational drug administration  
 budesonide: DT, drug therapy  
 budesonide: IH, inhalational drug administration  
 budesonide plus formoterol: DT, drug therapy  
 budesonide plus formoterol: IH, inhalational drug administration  
 beclometasone: DT, drug therapy  
 beclometasone: IH, inhalational drug administration  
 formoterol: DT, drug therapy  
 formoterol: IH, inhalational drug administration  
 cromoglycate disodium: DT, drug therapy  
 cromoglycate disodium: IH, inhalational drug administration  
 flunisolide: DT, drug therapy  
 flunisolide: IH, inhalational drug administration  
 prolair  
 formoterol fumarate  
 asthmasal  
 asthmabec  
 bemedrex

L99 ANSWER 6 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2002035497 EMBASE  
 TITLE: Chronic obstructive pulmonary disease: The GOLD initiative.  
 AUTHOR: Leuenberger P.; Rochat T.  
 CORPORATE SOURCE: Prof. P. Leuenberger, Division de Pneumologie, CHUV, 1011  
 Lausanne, Switzerland. philippe.leuenberger@chuv.hospvd.ch  
 SOURCE: Medecine et Hygiene, (9 Jan 2002) 60/2374 (54-62).  
 Refs: 42  
 ISSN: 0025-6749 CODEN: MEHGAB  
 COUNTRY: Switzerland  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 006 Internal Medicine  
 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Chronic obstructive pulmonary disease (COPD) is the object of a large  
 campaign of information and action among health professionals under the  
 acronym .mchlt.GOLD.mchgt. (Global initiative for Obstructive Lung  
 Disease). Tobacco smoke exposure is the main risk factor and tobacco  
 cessation is the most effective means to stop progression of the disease.  
 Pharmacological treatment is aimed at preventing and controlling the  
 symptoms and is based predominantly on the administration of  
 bronchodilators. The impact of inhaled corticosteroids on inflammation in  
 COPD is limited. Considering its significant side effects, maintenance  
 treatment with oral or intramuscular corticosteroids should be avoided.  
 Patient education and respiratory rehabilitation are important in the  
 management of patients with COPD. Long term oxygenotherapy prolongs  
 survival in the most severe patients. Chest surgery and lung  
 transplantation are to be restricted to carefully selected candidates.

CT Medical Descriptors:

\*chronic obstructive lung disease: DT, drug therapy  
 \*chronic obstructive lung disease: ET, etiology  
 \*chronic obstructive lung disease: PC, prevention  
 \*chronic obstructive lung disease: RH, rehabilitation  
 \*chronic obstructive lung disease: SU, surgery  
 health program  
 medical information  
 smoking

exposure  
risk factor  
smoking cessation  
disease course  
symptomatology  
drug efficacy  
corticosteroid therapy  
side effect: SI, side effect  
maintenance therapy  
patient education  
long term care  
oxygen therapy  
survival  
disease severity  
thorax surgery  
lung transplantation  
treatment indication  
    **aerosol**  
powder  
    **nebulization**  
assisted ventilation  
human  
controlled study  
article  
Drug Descriptors:  
tobacco smoke  
bronchodilating agent: DT, drug therapy  
bronchodilating agent: PR, pharmaceuticals  
bronchodilating agent: PD, pharmacology  
    **bronchodilating agent: IH, inhalational drug administration**  
corticosteroid: AE, adverse drug reaction  
corticosteroid: DT, drug therapy  
corticosteroid: PD, pharmacology  
    **corticosteroid: IH, inhalational drug administration**  
corticosteroid: IM, intramuscular drug administration  
corticosteroid: PO, oral drug administration  
oxygen: DT, drug therapy  
    **oxygen: IH, inhalational drug administration**  
beta 2 adrenergic receptor stimulating agent: DT, drug therapy  
beta 2 adrenergic receptor stimulating agent: PD, pharmacology  
salbutamol: DT, drug therapy  
salbutamol: PR, pharmaceuticals  
salbutamol: PD, pharmacology  
    **salbutamol: IH, inhalational drug administration**  
terbutaline: DT, drug therapy  
terbutaline: PR, pharmaceuticals  
terbutaline: PD, pharmacology  
    **terbutaline: IH, inhalational drug administration**  
fenoterol: DT, drug therapy  
fenoterol: PR, pharmaceuticals  
fenoterol: PD, pharmacology  
    **fenoterol: IH, inhalational drug administration**  
salmeterol xinafoate: DT, drug therapy  
salmeterol xinafoate: PR, pharmaceuticals  
salmeterol xinafoate: PD, pharmacology  
    **salmeterol xinafoate: IH, inhalational drug administration**  
formoterol fumarate: DT, drug therapy  
formoterol fumarate: PR, pharmaceuticals  
formoterol fumarate: PD, pharmacology  
    **formoterol fumarate: IH, inhalational drug administration**

cholinergic receptor blocking agent: DT, drug therapy  
cholinergic receptor blocking agent: PR, pharmaceuticals  
cholinergic receptor blocking agent: PD, pharmacology  
**cholinergic receptor blocking agent: IH, inhalational drug administration**  
ipratropium bromide: DT, drug therapy  
ipratropium bromide: PR, pharmaceuticals  
ipratropium bromide: PD, pharmacology  
**ipratropium bromide: IH, inhalational drug administration**  
methylxanthine: DT, drug therapy  
methylxanthine: PR, pharmaceuticals  
methylxanthine: PD, pharmacology  
**methylxanthine: IH, inhalational drug administration**  
aminophylline: DT, drug therapy  
aminophylline: PR, pharmaceuticals  
aminophylline: PD, pharmacology  
**aminophylline: IH, inhalational drug administration**  
theophylline: DT, drug therapy  
theophylline: PR, pharmaceuticals  
theophylline: PD, pharmacology  
**theophylline: IH, inhalational drug administration**  
glucocorticoid: DT, drug therapy  
antibiotic agent: DT, drug therapy  
Pneumococcus vaccine: DT, drug therapy  
alpha 1 antitrypsin: DT, drug therapy  
antioxidant: DT, drug therapy  
immunomodulating agent: DT, drug therapy  
antitussive agent: DT, drug therapy  
ambroxol: DT, drug therapy  
erdosteine: DT, drug therapy  
carbocisteine: DT, drug therapy  
salbutamol sulfate: DT, drug therapy  
salbutamol sulfate: PR, pharmaceuticals  
salbutamol sulfate: PD, pharmacology  
**salbutamol sulfate: IH, inhalational drug administration**  
**formoterol: DT, drug therapy**  
**formoterol: PD, pharmacology**  
**formoterol: IH, inhalational drug administration**

L99 ANSWER 7 OF 48 MEDLINE  
ACCESSION NUMBER: 2001435200 MEDLINE  
DOCUMENT NUMBER: 21191314 PubMed ID: 11296600  
TITLE: Long-acting asthma medication, new inhaler approved by FDA.  
AUTHOR: Thompson C A  
SOURCE: AMERICAN JOURNAL OF HEALTH-SYSTEM PHARMACY, (2001 Apr 1) 58  
(7) 557-8.  
Journal code: CBH; 9503023. ISSN: 1079-2082.  
PUB. COUNTRY: United States  
News Announcement  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010806  
Last Updated on STN: 20010806  
Entered Medline: 20010802  
CT Check Tags: Human  
\*Bronchodilator Agents: AD, administration & dosage  
\*Bronchodilator Agents: TU, therapeutic use  
Clinical Trials  
Device Approval

## Drug Approval

\*Ethanalamines: AD, administration &amp; dosage

\*Ethanalamines: TU, therapeutic use

## \*Nebulizers and Vaporizers

United States

United States Food and Drug Administration

L99 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:564809 CAPLUS

DOCUMENT NUMBER: 135:142240.

TITLE: A method of administering a medicinal aerosol formulation

INVENTOR(S): Adjei, Akwete L.; Stefanos, Simon; Zhu, Yaping

PATENT ASSIGNEE(S): Aeropharm Technology, Inc., USA

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054664	A1	20010802	WO 2001-US116	20010102
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-177982P P 20000125

US 2000-702194 A 20001030

AB A method of treating in a human or animal a condition capable of treatment by oral or nasal inhalation has been found. The method comprises administering a medicinal aerosol formulation comprising a selected medicament under conditions where the amt. of the selected drug delivered to the site of action, e.g. the lungs, is maximized. After intrapulmonary and i.v. administration of 7.5, and 5.0 .mu.g/kg amylin, resp., to rabbits the half life of the drug in the body was 26.38 and 17.17 min, resp.

CT Immunoglobulins

CT Immunoglobulins

CT Immunoglobulins

CT Immunoglobulins

CT Immunoglobulins

CT **Drug delivery systems**

CT Antibiotics

CT Antidiabetic agents

CT Albumins, biological studies

CT Cytokines

CT Interferons

CT Interleukins

CT Ovalbumin

CT Peptides, biological studies

CT Proteins, general, biological studies

CT Drug delivery systems

REFERENCE COUNT: 3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 9 OF 48 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:247172 CAPLUS  
 DOCUMENT NUMBER: 134:256899  
 TITLE: Combination of loteprednol and .beta.2-adrenoceptor agonists for the treatment of allergies and respiratory tract diseases  
 INVENTOR(S): Szelenyi, Istvan; Poppe, Hildegard; Heer, Sabine; Engel, Juergen  
 PATENT ASSIGNEE(S): Asta Medica Ag, Germany  
 SOURCE: PCT Int. Appl., 16 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022956	A2	20010405	WO 2000-EP9392	20000926
WO 2001022956	A3	20011011		

W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

DE 19947235 A1 20010405 DE 1999-19947235 19990930

PRIORITY APPLN. INFO.: DE 1999-19947235 A 19990930

AB The invention relates to a novel combination of a soft steroid, esp. loteprednol, and at least one .beta.2-adrenoceptor agonist for treating allergies and/or respiratory tract diseases simultaneously, sequentially or sep.; to drugs contg. said combination, to methods for producing such drugs and to the use of the novel combination for producing drugs for the simultaneous, sequential or sep. treatment of allergies and/or respiratory tract diseases. Thus and aerosol was prepd. that contained 6 .mu.g formoterol fumarate dihydrate and 200 .mu.g loteprednol per stroke. 2H-heptafluoropropane (1.000 g) propellant was cooled to -55.degree.C and 11.7 g Tagat TO in 11.7 g ethanol was added under stirring, followed by the addn. of 3.34 g micronized loteprednol etabonate and 0.1 g formoterol fumarate dihydrate. The suspension was dild. with 1,170.0 g 2H-heptafluoropropane, filled in metal containers with valves for dosing 50 .mu.L suspension per stroke.

CT Drug delivery systems  
 CT Drug delivery systems  
 CT Allergy  
 CT Steroids, biological studies  
 CT Respiratory tract  
 CT Drug delivery systems  
 CT Drug delivery systems  
 CT Adrenoceptor agonists

L99 ANSWER 10 OF 48 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:867964 CAPLUS  
 DOCUMENT NUMBER: 135:376803  
 TITLE: Stable pharmaceutical solution formulations for pressurized metered dose inhalers  
 INVENTOR(S): Lewis, David; Ganderton, David; Meakin, Brian; Brambilla, Gaetano; Ferraris, Alessandra  
 PATENT ASSIGNEE(S): Chiesi Farmaceutici S.P.A., Italy  
 SOURCE: Eur. Pat. Appl., 18 pp.

DOCUMENT TYPE: CODEN: EPXXDW  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: 1 English  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1157689	A1	20011128	EP 2001-112230	20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001089480	A1	20011129	WO 2000-EP4635	20000522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

US 2002025299 A1 20020228 US 2001-860689 20010521

PRIORITY APPLN. INFO.: WO 2000-EP4635 A 20000522

AB An aerosol soln. compn. for use in an aerosol inhaler comprises an active material, a propellant contg. a hydrofluoroalkane, a cosolvent and optionally a low volatility component to increase the mass median aerodynamic diam. (MMAD) of the aerosol particles on actuation of the inhaler. The active ingredient is a .beta.2 agonist selected from salbutamol, formoterol, salmeterol, and TA-2005, salts thereof or their combination with steroid such as beclomethasone dipropionate, fluticasone propionate, budesonide, and its 22R-epimer or an anticholinergic atropine-like deriv. such as ipratropium bromide, oxitropium bromide, and tiotropium bromide. The compn. is stabilized by using a small amt. of mineral acid and a suitable can having part or all of its internal metallic surfaces made of stainless steel, anodized aluminum or lined with an inert org. coating.

CT **Drug delivery systems**  
 CT Alcohols, biological studies  
 CT Phenolic resins, uses  
 CT Alkanes, biological studies  
 CT Fluoropolymers, uses  
 CT Perfluorocarbons  
 CT Medical goods  
 CT Acids, biological studies  
 CT Fatty acids, biological studies  
 CT Epoxy resins, uses  
 CT Polysulfones, uses  
 CT Polyethers, uses  
 CT Cholinergic antagonists  
 CT Glycols, biological studies  
 CT Steroids, biological studies  
 CT Adrenoceptor agonists

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 11 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001122259 EMBASE

TITLE: [Anti-asthma drugs].  
 MEDICAMENTS ANTI-ASTHMATIQUES.

AUTHOR: Devillier P.



CORPORATE SOURCE: P. Devillier, Lab. de Pharmacologie-Toxicologie, Hopital  
Maison Blanche, Centre Hospitalier Univ. de Reims, 51092  
Reims Cedex, France. devillier@chu-reims.fr

SOURCE: Revue du Praticien, (15 Mar 2001) 51/5 (523-531).  
Refs: 26  
ISSN: 0035-2640 CODEN: REPRA3

COUNTRY: France

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: French

SUMMARY LANGUAGE: English; French

AB With respect to their main mechanism of action, anti-asthma drugs are classified as bronchodilators or anti-inflammatory drugs. Inhaled .beta.2-agonists are the most effective bronchodilators. The short-acting .beta.2-agonists are used for the relief of acute symptoms whereas long-acting .beta.2-agonists are used on a regular basis, concomitantly with inhaled corticoids, for long-term control of symptoms. The other bronchodilators (methylxanthines or anticholinergics) may be used in addition to the inhaled .beta.2-agonists. The treatment of bronchial inflammation is required in mild to severe persistent asthma. Inhaled corticoids are the main anti-inflammatory drugs. They have a low risk of adverse events at usual dosages. Anti-leukotrienes belong to a new class of anti-inflammatory drugs represented by montelukast in France. This drug is orally administered, well tolerated and used in addition to inhaled corticoids. Cromones and ketotifen are used only in mild persistent asthma. Inhaled .beta.2-agonists, anti-leukotrienes and cromones are also used for prevention of exercise-induced asthma.

CT Medical Descriptors:

\*asthma: DT, drug therapy  
\*asthma: ET, etiology  
\*asthma: PC, prevention  
drug mechanism  
bronchodilatation  
antiinflammatory activity  
exercise induced asthma: DT, drug therapy  
exercise induced asthma: PC, prevention  
**nebulization**

human  
review

Drug Descriptors:

\*antiasthmatic agent: DT, drug therapy  
\*antiasthmatic agent: PD, pharmacology  
\***antiasthmatic agent: IH, inhalational drug administration**  
\*bronchodilating agent: DT, drug therapy  
\***bronchodilating agent: IH, inhalational drug administration**  
\*corticosteroid: CB, drug combination  
\*corticosteroid: DT, drug therapy  
\***corticosteroid: IH, inhalational drug administration**  
\*leukotriene receptor blocking agent: DT, drug therapy  
\*leukotriene receptor blocking agent: PD, pharmacology  
\*antiinflammatory agent: CB, drug combination  
\*antiinflammatory agent: DT, drug therapy  
methylxanthine: DT, drug therapy  
beta 2 adrenergic receptor stimulating agent: DT, drug therapy  
montelukast: CB, drug combination  
montelukast: DT, drug therapy  
montelukast: PO, oral drug administration  
cromoglycate disodium: DT, drug therapy

ketotifen: DT, drug therapy  
fenoterol: DT, drug therapy  
    **fenoterol: IH, inhalational drug administration**  
pirbuterol: DT, drug therapy  
    **pirbuterol: IH, inhalational drug administration**  
terbutaline: DT, drug therapy  
    **terbutaline: IH, inhalational drug administration**  
terbutaline: PO, oral drug administration  
salbutamol: DT, drug therapy  
    **salbutamol: IH, inhalational drug administration**  
salbutamol: PO, oral drug administration  
    **formoterol: DT, drug therapy**  
    **formoterol: IH, inhalational drug administration**  
salmeterol: DT, drug therapy  
    **salmeterol: IH, inhalational drug administration**  
bambuterol: DT, drug therapy  
bambuterol: PO, oral drug administration  
theophylline: DT, drug therapy  
bamifylline: DT, drug therapy  
ipratropium bromide: DT, drug therapy  
oxitropium bromide: DT, drug therapy  
combivent: DT, drug therapy  
beclometasone: DT, drug therapy  
    **beclometasone: IH, inhalational drug administration**  
flunisolide: DT, drug therapy  
    **flunisolide: IH, inhalational drug administration**  
budesonide: DT, drug therapy  
    **budesonide: IH, inhalational drug administration**  
fluticasone: DT, drug therapy  
    **fluticasone: IH, inhalational drug administration**  
nedocromil: DT, drug therapy  
pirbuterol acetate  
salbutamol sulfate  
asmasal  
buventol  
spreor  
    **formoterol fumarate**  
salmeterol xinafoate  
oxeol  
aminophylline  
tedralan  
xanthium  
beclometasone dipropionate  
beclone  
bemedrex  
prolair  
spir  
fluticasone propionate  
fluticasone propionate plus salmeterol  
nedocromil sodium  
ketotifen fumarate

L99 ANSWER 12 OF 48 MEDLINE  
ACCESSION NUMBER: 2002066100 MEDLINE  
DOCUMENT NUMBER: 21649185 PubMed ID: 11791690  
TITLE: In vitro aerosol performance and dose uniformity between  
the Foradile Aerolizer and the Oxis Turbuhaler.  
AUTHOR: Chew N Y; Chan H K  
CORPORATE SOURCE: Faculty of Pharmacy, University of Sydney, NSW, Australia.  
SOURCE: JOURNAL OF AEROSOL MEDICINE, (2001 Winter) 14 (4) 495-501.

JOURNAL code: 8809251. ISSN: 0894-2684.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: T  
ENTRY MONTH: 200202  
ENTRY DATE: Entered STN: 20020125  
Last Updated on STN: 20020202  
Entered Medline: 20020201

AB Dry powder inhalers for **eformoterol** fumarate dihydrate, a long-acting beta-2 agonist for bronchodilation, are currently available as the Foradile Aerolizer and the Oxis Turbuhaler. The two products are different in the formulation, the aerosol production mechanism, and the device resistance to air flow. These disparities are likely to lead to different aerosol characteristics. Our objective was to compare the in vitro performance of these two inhalers in producing **eformoterol** aerosols. Emitted dose uniformity was measured using a sampling apparatus described in the British Pharmacopoeia. Ten individual doses (dose number 2, 3, 15, 16, 30, 31, 45, 46, 59, and 60) of the entire content (60 doses) were collected from the Aerolizer and the Turbuhaler (six inhalers each). Particle size distribution of the aerosols generated by the two inhalers were measured by a multiple stage liquid impinger at four different air flows (30-120 L/min). **Eformoterol** collected from the sampling devices was measured by HPLC. Fine particles are those of  $< \text{or} = 1.7\text{-}5.0$  microm in size in the aerosols obtained by interpolation of the data at the specified air flow. The Aerolizer showed a slight dependence of the emitted dose on the air flow, with the average emitted dose increased from 80% (at 30 L/min) to 90% (at higher flows) of the 12-microg label claim as compared with 60% for the Turbuhaler. When the emitted dose was normalized by the average emitted dose value, the Aerolizer showed less variation in the normalized emitted dose uniformity than the Turbuhaler. At high air flows, 90 and 120 L/min, both inhalers produced similar amounts (4 microg) of fine particles in the aerosol per dose discharged. As the flow as decreased to 30 and 60 L/min, both inhalers produced significantly less fine particles ( $p < 0.05$ ), with the Oxis Turbuhaler producing lesser amounts than the Foradile Aerolizer. However, due to the different device resistance, comparing the inhaler performance at the same inspiratory effort may be more appropriate. At a comfortable effort of 40 cm H<sub>2</sub>O, the Foradile Aerolizer would produce a significantly higher fine particle mass in the aerosols. We conclude that the two inhalers were dissimilar in the emitted dose uniformity. The fine particle mass of **eformoterol** produced by the two inhalers was equivalent at high but not at low air flows. The disparities may be due to the difference in the formulation and the aerosol generation mechanism of the inhalers.

CT Check Tags: Comparative Study; Human; In Vitro; Support, Non-U.S. Gov't  
**Aerosols**  
\*Bronchodilator Agents: AD, administration & dosage  
\*Ethanolamines: AD, administration & dosage  
**\*Nebulizers and Vaporizers**  
Particle Size  
Powders

L99 ANSWER 13 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2001261542 EMBASE  
TITLE: Is there a need for another inhalative .beta.(2)-agonist besides formoterol in patients with asthma?  
AUTHOR: Matthys H.  
CORPORATE SOURCE: Prof. H. Matthys, Aerztl. Dir. Abt. Pneumologie, Robert Koch Klinik, Universitätsklinik, Hugstetterstr. 55, D-79106 Freiburg, Germany. matthys@med1.ukl.uni-freiburg.de

SOURCE: Respiration, (2001) 68/4 (432-437).  
Refs: 63  
ISSN: 0025-7931 CODEN: RESPBD

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
027 Biophysics, Bioengineering and Medical Instrumentation  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Formoterol can substitute the rapid- and short-acting .beta.(2)-agonists as well as the slow- and long-acting salmeterol. Therefore formoterol in a fixed combination with an inhalant steroid reduces the aerosol devices necessary for asthma control to only one, to be used for regular 'controller' and, as needed, 'rescue therapy'. The side effect profile of formoterol is comparable to the short-acting .beta.(2)-agonists which makes the combination with a topically active glucocorticoid applicable in patients of any asthma severity as long as they are able to perform an inspiratory vital capacity maneuver. Copyright .COPYRG. 2001 S. Karger AG, Basel.

CT Medical Descriptors:  
\*asthma: DI, diagnosis  
\*asthma: DT, drug therapy  
\*asthma: PC, prevention  
drug choice  
steroid therapy  
aerosol  
device  
drug delivery system  
disease control  
disease severity  
vital capacity  
inspiratory capacity  
prophylaxis  
diagnostic test  
drug safety  
drug induced disease: SI, side effect  
sustained release preparation  
drug formulation  
human  
clinical trial  
article  
priority journal  
Drug Descriptors:  
\*beta 2 adrenergic receptor stimulating agent: AE, adverse drug reaction  
\*beta 2 adrenergic receptor stimulating agent: CT, clinical trial  
\*beta 2 adrenergic receptor stimulating agent: AD, drug administration  
\*beta 2 adrenergic receptor stimulating agent: CB, drug combination  
\*beta 2 adrenergic receptor stimulating agent: CM, drug comparison  
\*beta 2 adrenergic receptor stimulating agent: DT, drug therapy  
\*beta 2 adrenergic receptor stimulating agent: PR, pharmaceuticals  
\*beta 2 adrenergic receptor stimulating agent: PD, pharmacology  
\*beta 2 adrenergic receptor stimulating agent: IH, inhalational drug administration  
\*formoterol: AE, adverse drug reaction  
\*formoterol: CT, clinical trial  
\*formoterol: AD, drug administration

\*formoterol: CB, drug combination  
\*formoterol: CM, drug comparison  
\*formoterol: DT, drug therapy  
\*formoterol: PR, pharmaceuticals  
\*formoterol: PD, pharmacology  
\*formoterol: IH, inhalational drug administration  
glucocorticoid: CB, drug combination  
glucocorticoid: DT, drug therapy  
glucocorticoid: PR, pharmaceuticals  
glucocorticoid: TP, topical drug administration  
steroid: CT, clinical trial  
steroid: AD, drug administration  
steroid: CB, drug combination  
steroid: DT, drug therapy  
steroid: PR, pharmaceuticals  
steroid: IH, inhalational drug administration  
steroid: PO, oral drug administration  
cholinergic receptor blocking agent: PD, pharmacology  
ipratropium bromide: PD, pharmacology  
tiotropium bromide: PD, pharmacology  
salmeterol: AE, adverse drug reaction  
salmeterol: CB, drug combination  
salmeterol: CM, drug comparison  
salmeterol: DT, drug therapy  
salmeterol: PR, pharmaceuticals  
salmeterol: PD, pharmacology  
fenoterol: AD, drug administration  
fenoterol: DT, drug therapy  
fenoterol: PR, pharmaceuticals  
fenoterol: PD, pharmacology  
fenoterol: IH, inhalational drug administration  
salbutamol: DT, drug therapy  
budesonide: CB, drug combination  
budesonide: DT, drug therapy  
budesonide: IH, inhalational drug administration  
theophylline: CB, drug combination  
theophylline: DT, drug therapy  
theophylline: PR, pharmaceuticals  
theophylline: PO, oral drug administration  
leukotriene receptor blocking agent: CB, drug combination  
leukotriene receptor blocking agent: DT, drug therapy  
leukotriene receptor blocking agent: PO, oral drug administration  
fluticasone: CB, drug combination  
fluticasone: DT, drug therapy  
fluticasone: PR, pharmaceuticals  
fluticasone: IH, inhalational drug administration  
formoterol fumarate: CB, drug combination  
formoterol fumarate: DT, drug therapy  
formoterol fumarate: PR, pharmaceuticals  
formoterol fumarate: IH, inhalational drug administration  
fluticasone propionate plus salmeterol: DT, drug therapy  
fluticasone propionate plus salmeterol: PR, pharmaceuticals  
fluticasone propionate plus salmeterol: IH, inhalational drug administration  
atmadisc  
discus  
foradil p  
miflonide  
seretide mite  
seretide forte

L99 ANSWER 14 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2001243038 EMBASE  
TITLE: Comparison of the anti-bronchoconstrictor activities of  
inhaled formoterol, its (R,R)- and (S,S)-enantiomers and  
salmeterol in the rhesus monkey.  
AUTHOR: Fozard J.R.; Buescher H.  
CORPORATE SOURCE: J.R. Fozard, Novartis Pharma AG., CH-4002 Basel,  
Switzerland. john\_r.fozard@pharma.novartis.com  
SOURCE: Pulmonary Pharmacology and Therapeutics, (2001) 14/4  
(289-295).  
Refs: 19  
ISSN: 1094-5539 CODEN: PPTHFJ  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The principle objective of this study was to define the  
anti-bronchoconstrictor effects of inhaled racemic formoterol and its  
(R,R)- and (S,S)-enantiomers in a new model of methacholine-induced  
bronchoconstriction in the rhesus monkey. A second long-acting .beta.(2)  
agonist, salmeterol, was included for comparison. Anaesthetized,  
spontaneously breathing rhesus monkeys were set up for measuring airway  
resistance. Blood pressure, heart rate and serum potassium concentrations  
were measured concomitantly to gauge systemic exposure and the potential  
for side effects. Formoterol, 0.14, 0.34 and 1.15 .mu.g/kg, administered  
by aerosol, induced rapidly developing, sustained, dose-related inhibition  
of the bronchoconstrictor responses to aerosolised methacholine (maximum  
76%) accompanied by sustained, dose-related tachycardia. (R,R)-formoterol,  
0.56 .mu.g/kg, induced anti-bronconstrictor effects and an associated  
tachycardia which corresponded closely to the effects seen following twice  
the dose of the racemate. (S,S)-formoterol, 0.54 .mu.g/kg, was inactive.  
Salmeterol, 1.4 .mu.g/kg, had no significant anti-bronchoconstrictor  
effect whereas doses of 5.5 and 30 .mu.g/kg produced quantitatively  
similar but submaximal anti-bronchoconstrictor effects (maximum 47%).  
Sustained dose-dependent tachycardia was seen with salmeterol over the  
full dose range. Thus, the anti-bronchoconstrictor activity of formoterol  
resides in the (R,R) enantiomer and the (S,S) enantiomer does not  
interfere with the activity when present in the racemic form. Furthermore,  
the data indicate that the present model of methacholine-induced  
bronchospasm in the rhesus monkey could be useful in defining the key  
properties of .beta.(2) agonist bronchodilators such as relative potency,  
efficacy, duration of action and potential for systemic side effects.  
.COPYRGT. 2001 Academic Press.

CT Medical Descriptors:  
enantiomer  
rhesus monkey  
drug activity  
drug effect  
bronchospasm  
airway resistance  
blood pressure  
heart rate  
potassium blood level  
aerosol  
tachycardia: CO, complication  
dose response

drug potency  
drug efficacy  
disease model  
nonhuman  
male  
animal experiment  
animal model  
controlled study  
article  
priority journal  
Drug Descriptors:

\*formoterol: CM, drug comparison  
\*formoterol: TO, drug toxicity  
\*formoterol: PD, pharmacology  
\*formoterol: IH, inhalational drug administration  
\*salmeterol: CM, drug comparison  
\*salmeterol: TO, drug toxicity  
\*salmeterol: PD, pharmacology  
\*salmeterol: IH, inhalational drug administration  
bronchodilating agent: TO, drug toxicity  
methacholine  
potassium: EC, endogenous compound

L99 ANSWER 15 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001406622 EMBASE

TITLE: Managing stable chronic obstructive pulmonary disease.

SOURCE: Drug and Therapeutics Bulletin, (2001) 39/11 (81-85).

Refs: 57

ISSN: 0012-6543 CODEN: DRTBAE

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

019 Rehabilitation and Physical Medicine

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Over 26,000 people died of chronic obstructive pulmonary disease (COPD) in England and Wales in 1999. The disease is a common cause of consultations in primary care and accounts for as many as 1 in 8 medical admissions. Patients with stable COPD, the focus of this article, experience chronic symptoms such as breathlessness, cough, sputum production, wheeze and chest tightness, which worsen slowly over time. We do not deal here with the management of severe acute exacerbations, which are caused by an additional (often infective) process.

CT Medical Descriptors:

\*chronic obstructive lung disease: DI, diagnosis

\*chronic obstructive lung disease: DT, drug therapy

\*chronic obstructive lung disease: RH, rehabilitation

\*chronic obstructive lung disease: SU, surgery

\*chronic obstructive lung disease: TH, therapy

patient care

mortality

United Kingdom

consultation

primary medical care

hospital admission

symptom

dyspnea  
coughing  
sputum  
wheezing  
thorax pain  
disease severity  
acute disease  
disease exacerbation  
lung infection: DT, drug therapy  
spirometry  
oxygen therapy  
medical nebulizer  
smoking cessation  
substitution therapy  
side effect: SI, side effect  
drug blood level  
metered dose inhaler  
dry powder  
drug delivery system  
    **nebulization**  
rehabilitation  
ambulatory care  
lung surgery  
lung transplantation  
travel  
human  
clinical trial  
randomized controlled trial  
controlled study  
article  
Drug Descriptors:  
\*oxygen: CT, clinical trial  
\*oxygen: DT, drug therapy  
nicotine: DT, drug therapy  
amfebutamone: DT, drug therapy  
bronchodilating agent: DT, drug therapy  
beta adrenergic receptor stimulating agent: CB, drug combination  
beta adrenergic receptor stimulating agent: DT, drug therapy  
beta adrenergic receptor stimulating agent: PD, pharmacology  
muscarinic receptor blocking agent: CB, drug combination  
muscarinic receptor blocking agent: DO, drug dose  
muscarinic receptor blocking agent: DT, drug therapy  
muscarinic receptor blocking agent: PR, pharmaceuticals  
muscarinic receptor blocking agent: PD, pharmacology  
    **muscarinic receptor blocking agent: IH, inhalational drug administration**  
theophylline: AE, adverse drug reaction  
theophylline: CB, drug combination  
theophylline: CR, drug concentration  
theophylline: DO, drug dose  
theophylline: IT, drug interaction  
theophylline: DT, drug therapy  
theophylline: PR, pharmaceuticals  
theophylline: PK, pharmacokinetics  
theophylline: PD, pharmacology  
theophylline: PO, oral drug administration  
salbutamol: CT, clinical trial  
salbutamol: CM, drug comparison  
salbutamol: DO, drug dose  
salbutamol: DT, drug therapy



salbutamol: PR, pharmaceuticals  
salbutamol: PD, pharmacology  
    **salbutamol: IH, inhalational drug administration**  
terbutaline: CT, clinical trial  
terbutaline: CM, drug comparison  
terbutaline: DO, drug dose  
terbutaline: DT, drug therapy  
terbutaline: PR, pharmaceuticals  
terbutaline: PD, pharmacology  
    **terbutaline: IH, inhalational drug administration**  
placebo  
ipratropium bromide: DO, drug dose  
ipratropium bromide: DT, drug therapy  
ipratropium bromide: PR, pharmaceuticals  
ipratropium bromide: PD, pharmacology  
    **ipratropium bromide: IH, inhalational drug administration**  
oxitropium bromide: DO, drug dose  
oxitropium bromide: DT, drug therapy  
oxitropium bromide: PR, pharmaceuticals  
oxitropium bromide: PD, pharmacology  
    **oxitropium bromide: IH, inhalational drug administration**  
salmeterol: CT, clinical trial  
salmeterol: CM, drug comparison  
salmeterol: DO, drug dose  
salmeterol: DT, drug therapy  
salmeterol: PR, pharmaceuticals  
salmeterol: PD, pharmacology  
    **salmeterol: IH, inhalational drug administration**  
    **formoterol: CT, clinical trial**  
    **formoterol: CM, drug comparison**  
    **formoterol: DO, drug dose**  
    **formoterol: DT, drug therapy**  
    **formoterol: PR, pharmaceuticals**  
    **formoterol: PD, pharmacology**  
    **formoterol: IH, inhalational drug administration**  
macrolide: IT, drug interaction  
macrolide: PD, pharmacology  
quinolone: IT, drug interaction  
quinolone: PD, pharmacology  
corticosteroid: CT, clinical trial  
corticosteroid: DO, drug dose  
corticosteroid: DT, drug therapy  
corticosteroid: PR, pharmaceuticals  
corticosteroid: PD, pharmacology  
    **corticosteroid: IH, inhalational drug administration**  
corticosteroid: PO, oral drug administration  
fluticasone: CT, clinical trial  
fluticasone: DO, drug dose  
fluticasone: DT, drug therapy  
fluticasone: PR, pharmaceuticals  
fluticasone: PD, pharmacology  
    **fluticasone: IH, inhalational drug administration**  
fluticasone: PO, oral drug administration  
budesonide: CT, clinical trial  
budesonide: DO, drug dose  
budesonide: DT, drug therapy  
budesonide: PR, pharmaceuticals  
budesonide: PD, pharmacology  
    **budesonide: IH, inhalational drug administration**  
budesonide: PO, oral drug administration

mucolytic agent: CT, clinical trial  
 mucolytic agent: DT, drug therapy  
 mucolytic agent: PD, pharmacology  
 mucolytic agent: PO, oral drug administration  
 carbocisteine: CT, clinical trial  
 carbocisteine: DT, drug therapy  
 carbocisteine: PD, pharmacology  
 carbocisteine: PO, oral drug administration  
 influenza vaccine: DT, drug therapy  
 Pneumococcus polysaccharide: DT, drug therapy  
 antibiotic agent: DT, drug therapy

L99 ANSWER 16 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001086626 EMBASE

TITLE: [Aerosol therapy in the new millennium: How to proceed  
 after the elimination of CFC-driven pMDI's containing  
 short-acting .beta.(2)-agonists].  
 INHALATIONSTHERAPIE IM NEUEN MILLENNIUM. WIE WEITER NACH  
 DEM VERBOT VON FCKW-HALTIGEN KURZWIRKSAMEN  
 .beta.(2)-AGONISTEN?..

AUTHOR: Matthys H.

CORPORATE SOURCE: Dr. H. Matthys, Abteilung Pneumologie, Universitätsklinikum  
 Freiburg, Hugstetter Strasse 55, D-79106 Freiburg, Germany  
 SOURCE: Atemwegs- und Lungenkrankheiten, (2001) 27/2 (79-84).

Refs: 26

ISSN: 0341-3055 CODEN: ATLUDF

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 027 Biophysics, Bioengineering and Medical  
 Instrumentation  
 037 Drug Literature Index

LANGUAGE: German

SUMMARY LANGUAGE: English; German

AB After the ban of CFC-driven metered dose inhalers (pMDI's) containing  
 short-acting .beta.(2)-agonists, there are 3 alternatives left for acute  
 reliever therapy of patients with asthma and chronic bronchitis: 1) Dry  
 powder inhalers with short-acting .beta.(2)-agonists or formoterol, 2)  
 HFA-driven pMDI's with short-acting .beta.(2)-agonists, 3) Nebulizers with  
 short-acting .beta.(2)-agonists solutions. The literature which supports  
 the use of formoterol as a reliever and controller drug substituting  
 short-acting .beta.(2)-agonists and salmeterol in one molecule is  
 discussed as well as the new hierarchy to prescribe aerosol therapy in  
 patients suffering reversible airway obstruction.

CT Medical Descriptors:

\*metered dose inhaler  
 \*asthma: DT, drug therapy  
 \*chronic bronchitis: DT, drug therapy  
 dry powder  
 nebulizer

**aerosol**

airway obstruction: DT, drug therapy  
 lung function  
 human  
 review

Drug Descriptors:

\*beta 2 adrenergic receptor stimulating agent: AD, drug administration  
 \*beta 2 adrenergic receptor stimulating agent: DT, drug therapy  
 \*beta 2 adrenergic receptor stimulating agent: IH, inhalational drug  
 administration

\*formoterol: AD, drug administration  
 \*formoterol: DT, drug therapy  
 \*formoterol: IH, inhalational drug administration  
 \*salmeterol: AD, drug administration  
 \*salmeterol: DT, drug therapy  
 \*salmeterol: IH, inhalational drug administration  
 terbutaline: AD, drug administration  
 terbutaline: DT, drug therapy  
 terbutaline: IH, inhalational drug administration  
 salbutamol: AD, drug administration  
 salbutamol: DT, drug therapy  
 salbutamol: IH, inhalational drug administration

L99 ANSWER 17 OF 48 MEDLINE  
 ACCESSION NUMBER: 2001492464 MEDLINE  
 DOCUMENT NUMBER: 21425858 PubMed ID: 11534896  
 TITLE: Pharmacological similarities and differences between  
 beta2-agonists.  
 AUTHOR: Lotvall J  
 CORPORATE SOURCE: Department of Respiratory Medicine and Allergology,  
 Goteborg University, Sweden.. lotvallj@mail.mednet.gu.se  
 SOURCE: RESPIRATORY MEDICINE, (2001 Aug) 95 Suppl B S7-11. Ref: 15  
 Journal code: RME; 8908438. ISSN: 0954-6111.  
 PUB. COUNTRY: England: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200109  
 ENTRY DATE: Entered STN: 20010906  
 Last Updated on STN: 20011001  
 Entered Medline: 20010927

AB Formoterol and salmeterol are both long-acting bronchodilators that are effective in the treatment of asthma. However, some differences exist in their pharmacology that are reflected in their clinical profiles. Formoterol has a rapid onset of action, whereas salmeterol causes bronchodilation in a somewhat slower manner. However, both of these drugs are long-acting. After single doses clear effects are maintained for 12 h after inhalation, and with high doses effects are observed even at 24 h. Differences between the maximal effects of both drugs are also a consequence of their pharmacological properties. Thus, formoterol has higher intrinsic activity than salmeterol, which means that it is a full agonist, whereas salmeterol is a partial agonist on the beta2-receptor. Physicochemical properties of the drugs may explain the differences in onset and duration of action. Adequate water solubility and moderate lipophilicity of formoterol ensures rapid diffusion to the beta2-receptor on the smooth muscle and rapid bronchodilating activity. Salmeterol, on the other hand, may diffuse more slowly to the beta2-receptor because of its high lipophilicity explaining the slower onset of action. Unlike salbutamol, which is hydrophilic and has a rapid onset and short duration of action, both formoterol and salmeterol possess adequate lipophilic properties to remain in the airway tissues as a depot in close vicinity to the beta2-receptor, explaining their long duration of effect. The long duration of salmeterol has also been suggested to depend on an anchored binding within the beta2-receptor. The pharmacological evidence for a rapid onset of action of formoterol, but long duration of effect, is supported by several clinical studies. The fast onset of bronchodilation and high intrinsic activity of formoterol therefore suggest that it can be used for relief treatment in patients with asthma

if they are concomitantly treated with inhaled glucocorticoids.

CT Check Tags: Animal; Human  
\*Adrenergic beta-Agonists: PD, pharmacology  
Albuterol: AA, analogs & derivatives  
\*Albuterol: PD, pharmacology  
\*Asthma: DT, drug therapy  
Blood Glucose: ME, metabolism  
Blood Pressure: DE, drug effects  
Bronchodilator Agents: PD, pharmacology  
Dose-Response Relationship, Drug  
\*Ethanolamines: PD, pharmacology  
Heart Rate: DE, drug effects  
Potassium: BL, blood  
Randomized Controlled Trials  
\*Receptors, Adrenergic, beta-2: DE, drug effects  
Terbutaline: PD, pharmacology  
Time Factors

L99 ANSWER 18 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-37397 DRUGU P T

TITLE: Pharmacological similarities and differences between  
beta-agonists.

AUTHOR: Lotvall J

CORPORATE SOURCE: Univ.Göteborg

LOCATION: Göteborg, Swed.

SOURCE: Respir.Med. (95, Suppl. B, S7-S11, 2001) 6 Fig. 1 Tab. 15  
Ref.

CODEN: RMEDE

ISSN: 0954-6111

AVAIL. OF DOC.: The Lung Pharmacology Group, Department of Respiratory  
Medicine and Allergology, Guldhedsgatan 10A, SE-413 46  
Göteborg, Sweden. (e-mail: lotvallj@mail.mednet.gu.se).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The pharmacological similarities and differences between beta-2-agonists  
is reviewed with reference to receptor interaction, onset of action and  
duration of effect and clinical profiles. Drugs mentioned include  
**formoterol** (FO), salmeterol (SA), salbutamol and terbutaline.  
Adequate **water** solubility and moderate lipophilicity of FO  
ensure rapid diffusion to the beta-2 receptor on the smooth muscle and  
rapid bronchodilating activity. SA may diffuse more slowly to the  
receptor due to high lipophilicity, with consequent slower onset of  
action. Salbutamol, which is hydrophilic, has a rapid onset and short  
duration of action. FO and SA having adequate lipophilic properties to  
remain in the airways, have a longer duration of effect. These  
pharmacological findings are supported clinically.

CT ASTHMA \*TR; PNEUMOPATHY \*TR; PNEUMOPATHY \*TR; SYMPATHOMIMETIC-BETA  
\*FT; IN-VIVO \*FT; REVIEW \*FT; RECEPTOR \*FT

[01] SYMPATHOMIMETICS-BETA \*FT; MAIN-TOPIC \*FT; ANTI-ASTHMATICS \*FT; PH \*FT

[02] **FORMOTEROL** \*PH; SALMETEROL \*PH; SALBUTAMOL \*PH; TERBUTALINE

\*PH; **FORMOTEROL** \*TR; SALMETEROL \*TR; SALBUTAMOL \*TR;

TERBUTALINE \*TR; ANTI-ASTHMATIC \*FT; PH \*FT; TR \*FT

L99 ANSWER 19 OF 48 CAPLUS COPYRIGHT 2002 ACS

DUPLICATE 1

ACCESSION NUMBER: 2000:573659 CAPLUS

DOCUMENT NUMBER: 133:168405

TITLE: Pharmaceuticals containing formoterol and a tiotropium  
salt

INVENTOR(S): Hassan, Ian Francis; Clarke, Jeremy Guy; Cuenoud,

PATENT ASSIGNEE(S): Bernard  
Novartis A.-G., Switz.; Novartis-Erfindungen  
Verwaltungsgesellschaft m.b.H.  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047200	A1	20000817	WO 2000-EP958	20000207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000008039	A	20011106	BR 2000-8039	20000207
EP 1158970	A1	20011205	EP 2000-902663	20000207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001003460	A	20010913	NO 2001-3460	20010712
PRIORITY APPLN. INFO.: GB 1999-2689 A 19990208				
WO 2000-EP958 W 20000207				
AB A compn. contains, sep. or together, formoterol or a pharmaceutically acceptable salt or a solvate of formoterol or the salt, and a tiotropium salt for simultaneous, sequential or sep. administration in the treatment of an inflammatory or obstructive airways disease. Thus, a dry powder formulation contained formoterol fumarate dihydrate 0.05, tiotropium bromide 0.05, and lactose monohydrate 99.90%.				
CT Drug delivery systems				
CT Drug delivery systems				
CT Respiratory tract				
CT Medical goods				
CT Anti-inflammatory agents				
CT Particle size distribution				
CT Carbohydrates, biological studies				
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L99 ANSWER 20 OF 48 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
ACCESSION NUMBER: 2000:401693 CAPLUS  
DOCUMENT NUMBER: 133:34456  
TITLE: A medicinal aerosol formulation  
INVENTOR(S): Adjei, Akwete; Cutie, Anthony J.  
PATENT ASSIGNEE(S): Aeropharm Technology Incorporated, USA  
SOURCE: PCT Int. Appl., 15 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

WO 2000033892 A1 20000615 WO 1999-US28644 19991203  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,  
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 US 6261539 B1 20010717 US 1998-209228 19981210  
 EP 1135173 A1 20010926 EP 1999-965104 19991203  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

US 1998-209228 A 19981210

WO 1999-US28644 W 19991203

AB This invention relates to a medicinal aerosol formulation and more particularly, to a medicinal aerosol formulation contg. a particulate drug, a propellant and a stabilizing agent comprising a water addn. Generally the formulations can be prepd. by combining (1) the drug, e.g. triamcinolone acetonide, in an amt. sufficient to provide a plurality of therapeutically EDS, (2) the water addn. in an amt. effective to stabilize each of the formulations, (3) the propellant in an amt. sufficient to propel a plurality of doses from an aerosol canister, and (4) any further optional components, e.g. ethanol as a cosolvent and dispersing the components.

CT Drug delivery systems

CT Drug delivery systems

REFERENCE COUNT: 1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 21 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:814297 CAPLUS

DOCUMENT NUMBER: 133:366421

TITLE: Pharmaceuticals containing (S,R)-formoterol

INVENTOR(S): Jerussi, Thomas P.; Senanayake, Chris Hugh

PATENT ASSIGNEE(S): Sepracor Inc., USA

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067741	A2	20001116	WO 2000-US12648	20000509
WO 2000067741	A3	20010315		
W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
US 2001007679	A1	20010712	US 1999-309154	19990510
US 6303145	B2	20011016		

PRIORITY APPLN. INFO.:

US 1999-309154 A 19990510

AB A method and compn. are disclosed utilizing the pure (S,R)-formoterol (I) isomer of formoterol, which is a bronchodilator with reduced adverse effects. I may be conveniently and safely formulated for aerosol administration. Thus, an inhalation aerosol contained I 180 mg, trichloromonofluoromethane 15.16, dichlorodifluoromethane 15.16, and sorbitan oleate 1.05 g.

CT **Drug delivery systems**  
 CT Drug delivery systems  
 CT Drug delivery systems  
 CT Gelatins, biological studies  
 CT Polysaccharides, biological studies  
 CT Drug delivery systems  
 CT Drug delivery systems  
 CT Adrenoceptors  
 CT Adrenoceptors  
 CT Adrenoceptors

L99 ANSWER 22 OF 48 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2000-579213 [54] WPIDS  
 DOC. NO. CPI: C2000-172401  
 TITLE: Medicament contains synergistic mixture of **formoterol** and mometasone furoate for treating inflammatory or obstructive airway diseases.  
 DERWENT CLASS: B01 B03  
 INVENTOR(S): CLARKE, J G; DANAHAY, H L; HASSAN, I F  
 PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH  
 COUNTRY COUNT: 91  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000051591	A1	20000908	(200054)*	EN	24
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000032843	A	20000921	(200065)		
NO 2001003988	A	20010816	(200169)		
EP 1156790	A1	20011128	(200201)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SK 2001001230	A3	20011203	(200203)		
BR 2000008699	A	20011226	(200206)		
CZ 2001003168	A3	20011212	(200206)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000051591	A1	WO 2000-EP1722	20000301
AU 2000032843	A	AU 2000-32843	20000301
NO 2001003988	A	WO 2000-EP1722	20000301
		NO 2001-3988	20010816
EP 1156790	A1	EP 2000-910739	20000301
		WO 2000-EP1722	20000301
SK 2001001230	A3	WO 2000-EP1722	20000301
		SK 2001-1230	20000301

BR 2000008699 A	BR 2000-8699	20000301
	WO 2000-EP1722	20000301
CZ 2001003168 A3	WO 2000-EP1722	20000301
	CZ 2001-3168	20000301

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000032843	A Based on	WO 200051591
EP 1156790	A1 Based on	WO 200051591
SK 2001001230	A3 Based on	WO 200051591
BR 2000008699	A Based on	WO 200051591
CZ 2001003168	A3 Based on	WO 200051591

PRIORITY APPLN. INFO: GB 1999-4919 19990303

AB WO 200051591 A UPAB: 20001027

NOVELTY - Medicament contains separately or together:

(a) **formoterol** or its salt or solvate; and  
 (b) mometasone furoate for simultaneous, sequential or separate administration in the treatment of an inflammatory or obstructive airway disease.

ACTIVITY - Antiinflammatory; respiratory; antiasthmatic. No activity data is given.

MECHANISM OF ACTION - None given.

USE - For treating inflammatory or obstructive airway diseases including asthma, acute lung injury, adult respiratory distress syndrome, pneumoconiosis and chronic obstructive pulmonary, airway or lung disease including chronic bronchitis and exacerbation of airways hyperactivity due to drug therapy.

ADVANTAGE - Combination is synergistic allowing reduction in amount of steroidal mometasone furoate to be significantly reduced and thus reducing risk of undesirable side effects.

Dwg.0/0

L99 ANSWER 23 OF 48 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-533078 [48] WPIDS

DOC. NO. CPI: C2000-158895

TITLE: Composition for treatment of inflammatory or obstructive airway diseases e.g. asthma or bronchitis, comprising **formoterol** and fluticasone propionate.

DERWENT CLASS: B01 B05

INVENTOR(S): CLARKE, J G; DANAHAY, H L; HASSAN, I F

PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH

COUNTRY COUNT: 91

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000048587	A1	20000824	(200048)*	EN	20
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES					
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS					
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL					
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000029115	A	20000904	(200103)		
NO 2001003987	A	20010816	(200169)		
BR 2000008276	A	20011106	(200175)		



CZ 2001002976 A3 20011114 (200175)  
 EP 1152753 A1 20011114 (200175) EN  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI  
 SK 2001001184 A3 20011203 (200203)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048587	A1	WO 2000-EP1270	20000216
AU 2000029115	A	AU 2000-29115	20000216
NO 2001003987	A	WO 2000-EP1270	20000216
		NO 2001-3987	20010816
BR 2000008276	A	BR 2000-8276	20000216
		WO 2000-EP1270	20000216
CZ 2001002976	A3	WO 2000-EP1270	20000216
		CZ 2001-2976	20000216
EP 1152753	A1	EP 2000-907572	20000216
		WO 2000-EP1270	20000216
SK 2001001184	A3	WO 2000-EP1270	20000216
		SK 2001-1184	20000216

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000029115	A Based on	WO 200048587
BR 2000008276	A Based on	WO 200048587
CZ 2001002976	A3 Based on	WO 200048587
EP 1152753	A1 Based on	WO 200048587
SK 2001001184	A3 Based on	WO 200048587

PRIORITY APPLN. INFO: GB 1999-3759 19990218

AB WO 200048587 A UPAB: 20001001

NOVELTY - A pharmaceutical composition comprises **formoterol** (A) or its salt or solvate and fluticasone propionate (B).

ACTIVITY - Antiinflammatory; antiasthmatic; antiallergic; expectorant. No activity example given.

MECHANISM OF ACTION - Beta-2 agonist.

USE - The composition can be used for the treatment of inflammatory or obstructive airway disease (claimed) e.g. asthma, acute lung injury, acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary-, airway- or lung- disease, chronic bronchitis, emphysema, bronchiectasis, airway hyper-reactivity and pneumoconiosis (e.g. asbestosis).

ADVANTAGE - The composition is synergistic and has rapid onset and long duration of action.

Dwg.0/0

L99 ANSWER 24 OF 48 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-182903 [16] WPIDS

DOC. NO. CPI: C2000-057396

TITLE: **Aerosol** propellant comprising dinitrogen monoxide and hydrofluoroalkane and optionally containing a pharmaceutically active substance.

DERWENT CLASS: A25 A96 B07

INVENTOR(S): HERZOG, K; KELLER, M; KRAUS, H; MUELLER-WALZ, R

PATENT ASSIGNEE(S): (JAGO-N) JAGO RESEARCH AG

COUNTRY COUNT: 28

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000006121	A1	20000210	(200016)*	GE	41
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA CN IN JP NO NZ US ZA					
AU 9945989	A	20000221	(200029)		
EP 1100465	A1	20010523	(200130)	GE	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 2001000391	A	20010323	(200130)		
ZA 2001000408	A	20010926	(200161)		42
CN 1312706	A	20010912	(200202)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000006121	A1	WO 1999-CH337	19990722
AU 9945989	A	AU 1999-45989	19990722
EP 1100465	A1	EP 1999-928996	19990722
		WO 1999-CH337	19990722
NO 2001000391	A	WO 1999-CH337	19990722
		NO 2001-391	20010123
ZA 2001000408	A	ZA 2001-408	20010115
CN 1312706	A	CN 1999-809683	19990722

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9945989	A Based on	WO 200006121
EP 1100465	A1 Based on	WO 200006121

PRIORITY APPLN. INFO: CH 1998-1565 19980724

AB WO 200006121 A UPAB: 20000330

NOVELTY - A compression-fluidized **aerosol** propellant comprising dinitrogen monoxide (I) and a hydrofluoroalkane (II) is new.

DETAILED DESCRIPTION - A compression-fluidized **aerosol** propellant comprising dinitrogen monoxide (I) and a hydrofluoroalkane of formula (II) is new.

$C_xH_yF_z$  (II)

$x = 1-3;$

$y$  and  $z =$  at least 1 and  $y + z = 2x + 2.$

INDEPENDENT CLAIMS are also included for:

(A) a medicinal **aerosol** formulation comprising the propellant and a pharmaceutically active substance; and

(B) the preparation of the formulation.

USE - The medicinal **aerosol** formulation is used especially for nasal and inhalative application. It is preferably filled into a pressure-tight container fitted with a dosage valve and an adapter for **nebulization** or inhalation.

ADVANTAGE - The propellant improves the wetting properties of pharmaceutically active substances and facilitates the production of suspension **aerosols** with improved suspension and stability properties and of solution **aerosols** with improved storage stability and reduced ethanol content. It also improves dosage accuracy and the adjustment of the particle size distribution as well as mass median aerodynamic diameter, increases the fine particle dose and lowers the oropharyngeal deposition.

Dwg.0/0

L99 ANSWER 25 OF 48 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2000-304726 [27] WPIDS  
 CROSS REFERENCE: 2000-294150 [26]; 2000-304725 [26]  
 DOC. NO. CPI: C2000-092694  
 TITLE: Stable concentrated liquid formulation of inhalable drug,  
 e.g. **formoterol** or salbutamol, in solution or  
 suspension medium, used after dilution for treatment of  
 respiratory disorders by inhalation.  
 DERWENT CLASS: B05 B07 P31 P33 P34 Q34  
 INVENTOR(S): HOCHRAINER, D; ZIERENBERG, B  
 PATENT ASSIGNEE(S): (BOEH) BOEHRINGER INGELHEIM PHARMA KG; (BOEH) BOEHRINGER  
 INGELHEIM PHARM AG; (HOCH-I) HOCHRAINER D; (ZIER-I)  
 ZIERENBERG B  
 COUNTRY COUNT: 52  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19847970	A1	20000420	(200027)*		7
WO 2000023037	A1	20000427	(200029)	GE	
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE					
W: AE AU BG BR CA CN CZ EE HR HU ID IL IN JP KR LT LV MX NO NZ PL RO					
SG SI SK TR UA US UZ VN YU ZA					
AU 9963370	A	20000508	(200037)		
BR 9914608	A	20010703	(200141)		
NO 2001001830	A	20010618	(200141)		
EP 1119334	A1	20010801	(200144)	GE	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE					
SI					
US 2001032643	A1	20011025	(200170)		
CZ 2001001363	A3	20011017	(200172)		
SK 2001000495	A3	20011106	(200176)		
KR 2001080187	A	20010822	(200213)		
CN 1323186	A	20011121	(200218)		
HU 2001003888	A2	20020228	(200223)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19847970	A1	DE 1998-19847970	19981017
WO 2000023037	A1	WO 1999-EP7589	19991009
AU 9963370	A	AU 1999-63370	19991009
BR 9914608	A	BR 1999-14608	19991009
		WO 1999-EP7589	19991009
NO 2001001830	A	WO 1999-EP7589	19991009
		NO 2001-1830	20010410
EP 1119334	A1	EP 1999-950688	19991009
		WO 1999-EP7589	19991009
US 2001032643	A1 Cont of	US 1999-416476	19991012
		US 2001-871500	20010531
CZ 2001001363	A3	WO 1999-EP7589	19991009
		CZ 2001-1363	19991009
SK 2001000495	A3	WO 1999-EP7589	19991009
		SK 2001-495	19991009
KR 2001080187	A	KR 2001-704780	20010416
CN 1323186	A	CN 1999-812222	19991009
HU 2001003888	A2	WO 1999-EP7589	19991009

HU 2001-3888

19991009

## FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9963370	A	Based on	WO 200023037
BR 9914608	A	Based on	WO 200023037
EP 1119334	A1		20 011110 DE 19847968
		Based on	WO 200023037
CZ 2001001363	A3	Based on	WO 200023037
SK 2001000495	A3	Based on	WO 200023037
HU 2001003888	A2	Based on	WO 200023037

PRIORITY APPLN. INFO: DE 1998-19847970 19981017; DE 1998-19847968  
19981017; US 1998-112380P 19981214

AB DE 19847970 A UPAB: 20020411

NOVELTY - A storage-stable formulation of drug(s) (I) effective on inhalation comprises a solvent or suspension medium and (I), where the concentration of (I) is 10-500 times the therapeutically effective concentration.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the use of the formulation for administration by inhalation, after 10-500 fold dilution.

ACTIVITY - Respiratory.

MECHANISM OF ACTION - Beta-mimetic.

USE - Use of the formulations for the treatment of respiratory diseases by inhalation is claimed; use in intranasal therapy is also mentioned in the disclosure.

ADVANTAGE - Stable **aqueous** liquid formulations are provided, which can be stored in the container of a **nebulizer** inhaler (especially in a two- or multi-chamber cartridge of a high pressure atomizer) for several months or even up to 5 years without reduction in pharmaceutical quality. The storage formulation can be converted simply and rapidly into an inhalation formulation.  
Dwg.0/0

L99 ANSWER 26 OF 48 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-294150 [26] WPIDS

CROSS REFERENCE: 2000-304725 [26]; 2000-304726 [26]

DOC. NO. CPI: C2000-089042

TITLE: Stable liquid formulation of **formoterol** in solution or suspension medium, used after dilution for treatment of asthma by inhalation.

DERWENT CLASS: B05

INVENTOR(S): HOCHRAINER, D; ZIERENBERG, B

PATENT ASSIGNEE(S): (BOEH) BOEHRINGER INGELHEIM PHARMA KG

COUNTRY COUNT: 52

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19847969	A1	20000420	(200026)*		7
WO 2000023065	A2	20000427	(200029)	GE	
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE					
W: AE AU BG BR CA CN CZ EE HR HU ID IL IN JP KR LT LV MX NO NZ PL RO					
SG SI SK TR UA US UZ VN YU ZA					
AU 9962019	A	20000508	(200037)		
US 6150418	A	20001121	(200101)		
NO 2001001663	A	20010403	(200137)		

BR 9914507 A 20010626 (200140)  
 EP 1121112 A2 20010808 (200146) GE  
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE  
 SI  
 CZ 2001001362 A3 20010912 (200158)  
 SK 2001000494 A3 20010911 (200159)  
 KR 2001075637 A 20010809 (200211)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19847969	A1	DE 1998-19847969	19981017
WO 2000023065	A2	WO 1999-EP7581	19991009
AU 9962019	A	AU 1999-62019	19991009
US 6150418	A	US 1999-416474	19991012
NO 2001001663	A	WO 1999-EP7581	19991009
		NO 2001-1663	20010403
BR 9914507	A	BR 1999-14507	19991009
		WO 1999-EP7581	19991009
EP 1121112	A2	EP 1999-948972	19991009
		WO 1999-EP7581	19991009
CZ 2001001362	A3	WO 1999-EP7581	19991009
		CZ 2001-1362	19991009
SK 2001000494	A3	WO 1999-EP7581	19991009
		SK 2001-494	19991009
KR 2001075637	A	KR 2001-704765	20010416

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9962019	A Based on	WO 200023065
BR 9914507	A Based on	WO 200023065
EP 1121112	A2 Based on	WO 200023065
CZ 2001001362	A3 Based on	WO 200023065
SK 2001000494	A3 Based on	WO 200023065

PRIORITY APPLN. INFO: DE 1998-19847969 19981017; US 1998-112380P  
 19981214

AB DE 19847969 A UPAB: 20020215

NOVELTY - A storage-stable **formoterol** (I) formulation comprises (I) (or its salt or addition product) at a concentration of 10-500 mg/ml (as (I)) in a solvent or suspension medium.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of the formulation for administration by inhalation, after dilution to a (I) concentration of 0.9-1.5 mg/ml.

ACTIVITY - Antiasthmatic; bronchodilator; hypoglycemic.

MECHANISM OF ACTION - beta 2 adrenergic stimulant; leukotriene release inhibitor; histamine release inhibitor.

USE - (I) is a beta 2 adrenergic stimulant, useful in the treatment of respiratory diseases, particularly asthma, by inhalation. Use of the formulations for the treatment of respiratory diseases by inhalation is claimed. (I) also shows hypoglycemic activity.

ADVANTAGE - A stable liquid formulation is provided, which can be stored in the container of a **nebulizer** inhaler (especially in a two- or multi-chamber cartridge of a high pressure atomizer) for several months or even several years without reduction in pharmaceutical quality. The storage formulation can be converted simply and rapidly into an inhalation formulation. (I) has previously only been used in powder form

for inhalative therapy in ambulant patients, due to its usual instability in solution.

Dwg.0/0

L99 ANSWER 27 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000213271 EMBASE

TITLE: [Formoterol Turbuhaler 6 .mu.g vs. Formoterol Aerolizer 12 .mu.g].  
FORMOTEROL TURBOHALER 6 .mu.G VS. FORMOTEROL AEROLIZER 12 .mu.G.

AUTHOR: Schlimmer P.

CORPORATE SOURCE: Dr. P. Schlimmer, Medizinische Klinik, SHG-Kliniken,  
D-66663 Merzig, Germany

SOURCE: Atemwegs- und Lungenkrankheiten, (2000) 26/5 (263-268).

Refs: 24

ISSN: 0341-3055 CODEN: ATLUDF

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
027 Biophysics, Bioengineering and Medical  
Instrumentation  
037 Drug Literature Index  
039 Pharmacy

LANGUAGE: German

SUMMARY LANGUAGE: English; German

AB Formoterol, a long lasting bronchodilator with a fast onset of action is available in two different devices, Turbuhaler and Aerolizer. Formoterol Turbuhaler 6 .mu.g contains a small amount of 0,594 .mu.g micronised lactose per dose whereas in the Aerolizer formoterol is combined with 22,5 mg grained lactose. Due to the differences in galenic composition and the properties of the inhalation devices, Turbuhaler deposits at least twice as much of the drug into the airways as compared with Aerolizer. In an open randomized crossover study design it was investigated whether the formoterol dose could be halved by using the Turbuhaler device and still produces a similar outcome regarding onset and duration of action and maximum effect. This was tested by measuring the specific airway conductance (sGAW) in asthmatic patients. After reversibility testing with terbutaline and a run-in period of one week 16 patients suffering from stable moderate to severe asthma were randomized. The patients inhaled a single dose of the different formulations on two different days. After the application of the drug sGAW was measured at different time points for a period of eight hours. No differences between the two types of formoterol inhalation devices were found regarding onset and duration of action, maximum effect and AUC. In conclusion it is possible to obtain a similar clinical effect with Formoterol Turbuhaler 6 .mu.g as with twice the dose in Formoterol Aerolizer 12 .mu.g. Beside the easier way of application Formoterol Turbuhaler 6 .mu.g provides the more economical alternative as well.

CT Medical Descriptors:

\*drug delivery system

\*asthma: DT, drug therapy

drug formulation

airway conductance

area under the curve

aerosol

drug distribution

treatment outcome

drug efficacy

human

clinical trial

randomized controlled trial  
crossover procedure  
controlled study  
article

## Drug Descriptors:

\*formoterol: CT, clinical trial  
\*formoterol: DT, drug therapy  
\*formoterol: IH, inhalational drug administration

L99 ANSWER 28 OF 48 MEDLINE DUPLICATE 3  
ACCESSION NUMBER: 2000213083 MEDLINE  
DOCUMENT NUMBER: 20213083 PubMed ID: 10751031  
TITLE: Hollow porous particles in metered dose inhalers.  
AUTHOR: Dellamary L A; Tarara T E; Smith D J; Woelk C H; Adractas  
A; Costello M L; Gill H; Weers J G  
CORPORATE SOURCE: Alliance Pharmaceutical Corp., San Diego, California 92121,  
USA.  
SOURCE: PHARMACEUTICAL RESEARCH, (2000 Feb) 17 (2) 168-74.  
Journal code: PHS; 8406521. ISSN: 0724-8741.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000616  
Last Updated on STN: 20000616  
Entered Medline: 20000605

AB PURPOSE: To assess the physical stability and aerosol characteristics of  
suspensions of hollow porous microspheres (PulmoSpheres) in HFA-134a.  
METHODS: Cromolyn sodium, albuterol sulfate, and **formoterol**  
fumarate microspheres were prepared by a spray-drying method. Particle  
size and morphology were determined via electron microscopy. Particle  
aggregation and suspension creaming times were assessed visually, and  
aerosol performance was determined via Andersen cascade impaction and dose  
uniformity studies. RESULTS: The hollow porous particle morphology allows  
the propellant to permeate freely within the particles creating a novel  
form of suspension termed a homodispersion, wherein the dispersed and  
continuous phases are identical, separated by an insoluble interfacial  
layer of drug and excipient. Homodispersion formation improves suspension  
stability by minimizing the difference in density between the particles  
and the medium, and by reducing attractive forces between particles. The  
improved physical stability leads to excellent dose uniformity. Excellent  
aerosolization efficiencies are also observed with PulmoSpheres  
formulations, with fine particle fractions of about 70%. CONCLUSIONS: The  
formation of hollow porous particles provides a new formulation technology  
for stabilizing suspensions of drugs in hydrofluoroalkane propellants with  
improved physical stability, content uniformity, and aerosolization  
efficiency.

CT Check Tags: Human; In Vitro  
Administration, Inhalation  
**Aerosols**  
Albuterol: AD, administration & dosage  
Albuterol: PK, pharmacokinetics  
\*Anti-Asthmatic Agents: AD, administration & dosage  
Anti-Asthmatic Agents: PK, pharmacokinetics  
\*Asthma: DT, drug therapy  
Bronchodilator Agents: AD, administration & dosage  
Bronchodilator Agents: PK, pharmacokinetics  
\*Cromolyn Sodium: AD, administration & dosage  
Cromolyn Sodium: PK, pharmacokinetics

Ethanolamines: AD, administration & dosage  
 Ethanolamines: PK, pharmacokinetics  
 Lung  
 Microscopy, Electron  
 Microspheres  
**\*Nebulizers and Vaporizers**  
 Particle Size  
 Powders

L99 ANSWER 29 OF 48 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1999-277187 [23] WPIDS  
 DOC. NO. NON-CPI: N1999-207801  
 DOC. NO. CPI: C1999-081380  
 TITLE: Unit for therapeutic liquid **aerosol** delivery to  
 respiratory system.  
 DERWENT CLASS: B05 B07 P34 Q32  
 INVENTOR(S): REDMON, M P; WEST, J A  
 PATENT ASSIGNEE(S): (SEPR-N) SEPRACOR INC  
 COUNTRY COUNT: 83  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9917754	A1	19990415	(199923)*	EN	24
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9896879	A	19990427	(199936)		
EP 1021172	A1	20000726	(200037)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 2000001747	A	20000405	(200039)		
CZ 2000001249	A3	20000816	(200048)		
US 6161536	A	20001219	(200102)		
HU 2000003917	A2	20010328	(200124)		
KR 2001024453	A	20010326	(200161)		
JP 2001518494	W	20011016	(200176)		27
AU 743174	B	20020117	(200219)		
EP 1021172	B1	20020410	(200227)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9917754	A1	WO 1998-US21115	19981007
AU 9896879	A	AU 1998-96879	19981007
EP 1021172	A1	EP 1998-950974	19981007
		WO 1998-US21115	19981007
NO 2000001747	A	WO 1998-US21115	19981007
		NO 2000-1747	20000405
CZ 2000001249	A3	WO 1998-US21115	19981007
		CZ 2000-1249	19981007
US 6161536	A Provisional	US 1997-61363P	19971008
		US 1998-168216	19981007
HU 2000003917	A2	WO 1998-US21115	19981007
		HU 2000-3917	19981007
KR 2001024453	A	KR 2000-703759	20000407



JP 2001518494 W		WO 1998-US21115	19981007
		JP 2000-514626	19981007
AU 743174	B	AU 1998-96879	19981007
EP 1021172	B1	EP 1998-950974	19981007
		WO 1998-US21115	19981007

## FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9896879	A	Based on	WO 9917754
EP 1021172	A1	Based on	WO 9917754
CZ 2000001249	A3	Based on	WO 9917754
HU 2000003917	A2	Based on	WO 9917754
JP 2001518494	W	Based on	WO 9917754
AU 743174	B	Previous Publ.	AU 9896879
		Based on	WO 9917754
EP 1021172	B1	Based on	WO 9917754

PRIORITY APPLN. INFO: US 1997-61363P 19971008; US 1998-168216  
19981007

AB WO 9917754 A UPAB: 20011203

NOVELTY - The unit has a solid state open matrix of a medicament and a **water** soluble or **water** dispersible carrier material contained in a **water** impermeable container.

DETAILED DESCRIPTION - The unit has a solid state open matrix of a medicament and a **water** soluble or **water** dispersible carrier material contained in a **water** impermeable container (16) and sufficient **water** to dissolve the matrix within fifteen seconds, contained in the second **water** impermeable container. The containers can be chambers within one housing. The unit also comprises a metered dose **nebulizer** (4).

USE - In respiratory therapy for topical administration of medication to the mucosal linings of the tracheobronchial tree.

ADVANTAGE - It is not necessary to pre-prepare the **aqueous** solution thus eliminating degradation and the need for low temperature storage.

DESCRIPTION OF DRAWING(S) - The drawing shows

**Nebulizer 4**

Container 16

Dwg.1/3

L99 ANSWER 30 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENTDUPLICATE 4

ACCESSION NUMBER: 1999-40431 DRUGU P S

TITLE: Mass balance and metabolism of 3H-**formoterol** in healthy men after combined i.v. and oral administration-mimicking inhalation.

AUTHOR: Rsenborg J; Larsson P; Tegner K; Hallstrom G

CORPORATE SOURCE: Astra-Zenaca; Univ.Uppsala

LOCATION: Lund; Uppsala, Swed.

SOURCE: Drug Metab.Dispos. (27, No. 10, 1104-16, 1999) 14 Fig. 2 Tab.  
21 Ref.

CODEN: DMDSAI ISSN: 0090-9556

AVAIL. OF DOC.: Experimental Medicine, AstraZeneca R&D, S-221 87 Lund, Sweden. (e-mail: johan.rosenborg@astrazeneca.com).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Combined p.o. + i.v. doses of the bronchodilator **formoterol**

(FO) given by a scheme simulating the fate of inhaled doses were followed by urinary and a lesser extent of fecal elimination in a study of 6 healthy men. The following metabolites were identified: FG1 and FG2 were glucuronides, FS was FO sulfate, Met1 was O-demethylformoterol, Met1G1 and Met1G2 were glucuronides of Met1, and Met2S was a sulfate of deformedylated FO (deformedylated FO, i.e., Met2, was not detected). FO, FG1, Met1G2 and FG2 were the major urinary metabolites while FO and Met1 were the major fecal metabolites; most plasma exposure was due to FO, FG1, Met1G2 and FG2. The data were used to propose a metabolic pathway for FO. Side-effects included mild palpitations in 4 subjects, lasting 5-28 min.

CT [01] **FORMOTEROL** \*DM; **FORMOTEROL** \*AE; PALPITATION \*AE;  
ARRHYTHMIA \*AE; CARDIOPATHY \*AE; FORMOTERO \*RN; P.O. \*FT; I.V. \*FT;  
BLOOD-PLASMA \*FT; CONC. \*FT; HALF-LIFE \*FT; TRITIUM-LABELED \*FT;  
METABOLITE \*FT; HUMAN \*FT; IN-VIVO \*FT; ELIMINATION \*FT; URINE \*FT;  
FECES \*FT; INJECTION \*FT; PHARMACOKINETICS \*FT; ANTI-ASTHMATICS \*FT;  
BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; DM \*FT; AE \*FT  
RN: 73573-87-2

L99 ANSWER 31 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-38625 DRUGU P

TITLE: Comparative biophysical analysis of the interaction of  
bronchodilating beta2-adrenoceptor agonists with lipid  
membranes.

AUTHOR: Ochsner M; Jaekel K; Mutz M; Anderson G P; John E

CORPORATE SOURCE: Univ.Basle; Novartis; Univ.Melbourne

LOCATION: Basle, Switz.; Melbourne, Austr.

SOURCE: Eur.J.Med.Chem. (34, No. 6, 451-62, 1999) 4 Fig. 3 Tab. 59  
Ref.

CODEN: EJMCAS ISSN: 0223-5234

AVAIL. OF DOC.: Biomedical Physics, Faculty of Medicine, University of Basel,  
Romergrasse 5, VH-4058 Basel, Switzerland.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Extensive analysis of the physicochemical properties of salmeterol (SM) and **formoterol** (FO; both Novartis Pharma) in comparison with the short acting beta-2 adrenoceptor agonist salbutamol (SB; Sigma) was carried out and a thorough characterization of drug interaction with lipid membranes was presented. The long-acting relaxant effects of these drugs was explained in terms of their accumulation within plasmalemma lipid bilayers of airway smooth muscle; the delayed response of SM was due to its higher lipophilicity. It was concluded that the drugs, having partitioned into the membrane lipid bilayer remain trapped and available to interact with beta-2 adrenoceptors. For SM, the majority of drug molecules approach the active site(s) of the receptor glycoproteins by lateral diffusion via the plasma membrane and poorly bind to the receptors from the extracellular space.

CT SALBUTAMOL \*RC; PARTITION-COEFFICIENT \*FT; ART.MEMBRANE \*FT;  
LIPOPHILICITY \*FT; ENTHALPY \*FT; ENTROPY \*FT; ADRENERGIC-RECEPTOR \*FT;  
BETA-2 \*FT; MODE-OF-ACT. \*FT; IN-VITRO \*FT; FLUORESCENCE \*FT;  
ANISOTROPY \*FT; LIPID \*FT; MEMBRANE \*FT; MESANGIAL-CELL \*FT;  
TISSUE-CULTURE \*FT; THERMODYNAMICS \*FT; RECEPTOR \*FT; SUBCELL.STRUCT.  
\*FT

[01] **FORMOTEROL** \*OC; **FORMOTEROL** \*PH; NOVARTIS \*FT;  
FORMOTERO \*RN; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT;  
SYMPATHOMIMETICS-BETA \*FT; OC \*FT; PH \*FT

RN: 73573-87-2

[02] SALMETEROL \*OC; SALMETEROL \*PH; NOVARTIS \*FT; SALMETERO \*RN;

BRONCHODILATORS \*FT; ANTI-ASTHMATICS \*FT; SYMPATHOMIMETICS-BETA \*FT; OC  
 \*FT; PH \*FT  
 RN: 89365-50-4

L99 ANSWER 32 OF 48 MEDLINE  
 ACCESSION NUMBER: 2000042498 MEDLINE  
 DOCUMENT NUMBER: 20042498 PubMed ID: 10572207  
 TITLE: Similar bronchodilation with **formoterol** delivered  
 by aerolizer or turbuhaler.  
 AUTHOR: Lotvall J; Mellen A; Arvidsson P; Palmqvist M; Radielovic  
 P; Kottakis J; Pfister P  
 CORPORATE SOURCE: Goteborg University, Sahlgrenska University Hospital,  
 Goteborg, Sweden.. jan.lotvall@mailier.mednet.gu.se  
 SOURCE: CANADIAN RESPIRATORY JOURNAL, (1999 Sep-Oct) 6 (5) 412-6.  
 Journal code: C1W; 9433332. ISSN: 1198-2241.  
 PUB. COUNTRY: Canada  
 (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RANDOMIZED CONTROLLED TRIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199912  
 ENTRY DATE: Entered STN: 20000113  
 Last Updated on STN: 20000113  
 Entered Medline: 19991214

AB BACKGROUND: In many countries, two dry powder formulations of inhaled  
**formoterol** are available for clinical use; one uses a single-dose  
 device (Foradil, Aerolizer), and the other uses a multiple-dose device  
 (Oxis, Turbuhaler). OBJECTIVES: To study the bronchodilating effect of  
**formoterol** 12 mg when delivered via the Aerolizer and Turbuhaler  
 devices over 12 h. STUDY DESIGN: Randomized, double-blind, placebo  
 controlled crossover study. Forced expiratory volume in one second (FEV1)  
 was monitored during a 12 h period. PATIENTS: Nineteen nonsmoking asthma  
 patients were included in the trial on the basis of reversibility of  
 symptoms in response to inhaled salbutamol (either 200 or 400 mg given  
 cumulatively; minimum reversibility 15%). RESULTS: There were no  
 significant differences between the two dry powder devices regarding the  
 change from baseline of FEV1 over 12 h, the area under the curve of FEV1  
 over 12 h or the maximum value of FEV1. The improvement in FEV1 with  
**formoterol** 12 mg versus placebo was highly significant for both  
 devices. CONCLUSIONS: **Formoterol** is similarly effective when  
 used as a dry powder when given by either Aerolizer or the Turbuhaler.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
 Administration, Inhalation

#### Aerosols

\*Asthma: DT, drug therapy  
 \*Bronchodilator Agents: AD, administration & dosage  
 Bronchodilator Agents: TU, therapeutic use  
 Cross-Over Studies  
 Double-Blind Method  
 \*Ethanolamines: AD, administration & dosage  
 Ethanolamines: TU, therapeutic use  
 Forced Expiratory Volume  
 Middle Age  
 \*Nebulizers and Vaporizers  
 Powders

L99 ANSWER 33 OF 48 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2000022720 EMBASE  
 TITLE: [High dose corticosteroids in spray in the treatment of

serious bronchial asthma].  
CORTICOSTEROIDES NEBULIZADOS EN ALTAS DOSIS EN EL  
TRATAMIENTO DEL ASMA BRONQUIAL GRAVE.

AUTHOR: Rivera J.M.O.  
CORPORATE SOURCE: J.M.O. Rivera, Seccion de Alergologia, Hospital Virgen del  
Camino-CS, Conde Oliveto, Pamplona, Spain  
SOURCE: Alergologia e Inmunologia Clinica, (1999) 14/4 (277-281).  
Refs: 12  
ISSN: 1575-734X CODEN: AICLF4  
COUNTRY: Spain  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
026 Immunology, Serology and Transplantation  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: Spanish  
CT Medical Descriptors:  
\*asthma: DT, drug therapy  
\*corticosteroid therapy  
disease severity  
drug indication  
drug megadose  
bronchodilatation  
    **nebulization**  
medical nebulizer  
combination chemotherapy  
drug efficacy  
human  
male  
female  
clinical article  
clinical trial  
controlled study  
adult  
conference paper  
Drug Descriptors:  
\*corticosteroid: CT, clinical trial  
\*corticosteroid: AD, drug administration  
\*corticosteroid: CB, drug combination  
\*corticosteroid: DO, drug dose  
\*corticosteroid: DT, drug therapy  
\*corticosteroid: PD, pharmacology  
    **\*corticosteroid: IH, inhalational drug administration**  
\*corticosteroid: PO, oral drug administration  
\*budesonide: CT, clinical trial  
\*budesonide: AD, drug administration  
\*budesonide: CB, drug combination  
\*budesonide: DO, drug dose  
\*budesonide: DT, drug therapy  
\*budesonide: PD, pharmacology  
    **\*budesonide: IH, inhalational drug administration**  
\*budesonide: PO, oral drug administration  
\*salbutamol: CT, clinical trial  
\*salbutamol: CB, drug combination  
\*salbutamol: DT, drug therapy  
\*salbutamol: PD, pharmacology  
    **\*salbutamol: IH, inhalational drug administration**  
theophylline: DT, drug therapy  
theophylline: PD, pharmacology  
    **formoterol: DT, drug therapy**

**formoterol: PD, pharmacology**  
salmeterol: DT, drug therapy  
salmeterol: PD, pharmacology

L99 ANSWER 34 OF 48 MEDLINE  
ACCESSION NUMBER: 1999109767 MEDLINE  
DOCUMENT NUMBER: 99109767 PubMed ID: 9893769  
TITLE: Onset and duration of action of single doses of  
**formoterol** inhaled via Turbuhaler.  
AUTHOR: Ringdal N; Derom E; Wahlin-Boll E; Pauwels R  
CORPORATE SOURCE: Medical Department, Fylkessykhuset i Molde, Norway.  
SOURCE: RESPIRATORY MEDICINE, (1998 Aug) 92 (8) 1017-21.  
Journal code: RME; 8908438. ISSN: 0954-6111.  
PUB. COUNTRY: ENGLAND: United Kingdom  
(CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199901  
ENTRY DATE: Entered STN: 19990216  
Last Updated on STN: 19990216  
Entered Medline: 19990129

AB The aim of the study was to investigate the time of onset and the duration of the bronchodilating effect of different doses of **formoterol** administered via Turbuhaler in patients with moderate asthma. Thirty-one patients (five women) with a mean forced expiratory volume in 1 s (FEV1) of 1.97 +/- 0.54 l and a mean reversibility of 31 +/- 14% of baseline were included in this double-blind, randomized, placebo-controlled and cross-over study. The patients inhaled single doses of placebo, i.e. 6, 12, 24, or 48 micrograms **formoterol** fumarate, on 5 separate days. Serial measurements of specific airways conductance (SGAW) and FEV1 were performed at regular time intervals for 12 h. The majority of the patients had at least a 50% increase in SGAW within 1-4 min after administration of all active treatments. The maximum increase in FEV1 over placebo was dose-dependent: 12% (6 micrograms), 18% (12 micrograms), 19% (24 micrograms), and 26% (48 micrograms) (P < 0.001). Twelve hours after administration of 6, 12, 24, and 48 micrograms **formoterol**, the mean increase in FEV1 was still 7%, 15%, 18%, and 27%, respectively, above the value following placebo. Headache was the most frequently reported adverse event in all treatments including placebo. After inhalation of 48 micrograms, three patients experienced mild tremor lasting for less than 1 h; likewise, one patient experienced the same event for 3 h after placebo. **Formoterol** administered via Turbuhaler10 gave a rapid and dose-related bronchodilating effect lasting for 12 h and was well tolerated.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Adolescence  
\*Adrenergic beta-Agonists: AD, administration & dosage  
Adrenergic beta-Agonists: PD, pharmacology  
Adult  
Aged  
\*Asthma: DT, drug therapy  
Asthma: PP, physiopathology  
\*Bronchodilator Agents: AD, administration & dosage  
Bronchodilator Agents: PD, pharmacology  
Cross-Over Studies  
Dose-Response Relationship, Drug  
Double-Blind Method  
\*Ethanolamines: AD, administration & dosage

Ethanolamines: PD, pharmacology  
 Forced Expiratory Volume: DE, drug effects  
 Middle Age  
**\*Nebulizers and Vaporizers**

L99 ANSWER 35 OF 48 MEDLINE  
 ACCESSION NUMBER: 97457702 MEDLINE  
 DOCUMENT NUMBER: 97457702 PubMed ID: 9311511  
 TITLE: Flow-dependent effect of **formoterol** dry-powder inhaled from the Aerolizer.  
 AUTHOR: Nielsen K G; Skov M; Klug B; Ifversen M; Bisgaard H  
 CORPORATE SOURCE: Dept of Paediatrics, National University Hospital, Copenhagen, Denmark.  
 SOURCE: EUROPEAN RESPIRATORY JOURNAL, (1997 Sep) 10 (9) 2105-9.  
 Journal code: ERY; 8803460. ISSN: 0903-1936.  
 PUB. COUNTRY: Denmark  
 (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RANDOMIZED CONTROLLED TRIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199712  
 ENTRY DATE: Entered STN: 19980109  
 Last Updated on STN: 19980109  
 Entered Medline: 19971201

AB The output and size distribution of aerosols from dry powder inhalers are dependent on the flow rate through the device. Therefore, in an in vivo study, we examined the flow-dependency of the effect of **formoterol** when delivered from a dry powder inhaler, the Aerolizer, in a flow range relevant to schoolchildren. In a preliminary study comprising 126 asthmatic children aged 3-10 yrs, the relationship between age and peak inspiratory flow (PIF) rate through the Aerolizer was determined. Mean PIF was 104 L.min<sup>-1</sup> and all children aged > 5 yrs performed a PIF > 60 L.min<sup>-1</sup>. Sixteen children aged 8-15 yrs with exercise-induced asthma (EIA) took part in the main trial comparing the protective effect of 12 micrograms **formoterol** inhaled at 60 and 120 L.min<sup>-1</sup>. The effect from high and low inspiratory flow was judged from the protective effect against EIA 12 h after drug administration. The decrease in forced expiratory volume in one second (FEV<sub>1</sub>) after exercise was 34% on the placebo day, but only 15% when **formoterol** was inhaled at the high flow rate. This difference was statistically significant. The decrease in FEV<sub>1</sub> was 23% after treatment with **formoterol** inhaled at the low flow rate, that was not significantly different from placebo or from high-flow **formoterol** treatment. These clinical findings correspond with the in vitro findings of flow-dependent fine particle mass from the Aerolizer, and corroborate the relationship between fine particle mass of aerosol and clinical effect. The results indicate a flow-dependent effect of **formoterol** dry powder inhaled from the Aerolizer, within the range of inspiratory flow rate obtainable by school-children. This questions its applicability in children with asthma.

CT Check Tags: Female; Human; Male  
 Administration, Inhalation  
 Adolescence  
 \*Asthma, Exercise-Induced: DT, drug therapy  
 Asthma, Exercise-Induced: PP, physiopathology  
 \*Bronchodilator Agents: AD, administration & dosage  
 Child  
 Child, Preschool  
 Cross-Over Studies  
 Double-Blind Method

\*Ethanolamines: AD, administration & dosage  
Forced Expiratory Volume: DE, drug effects  
\*Nebulizers and Vaporizers  
Powders  
Pulmonary Ventilation: DE, drug effects

L99 ANSWER 36 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1997-11601 DRUGU C

TITLE: Enantio- and diastereoselective synthesis of all four stereoisomers of formoterol.

AUTHOR: Hett R; Fang Q K; Gao Y; Hong Y; Butler H T; Nie X; Wald S A

CORPORATE SOURCE: Sepracor

LOCATION: Marlborough, Mass., USA

SOURCE: Tetrahedron Lett. (38, No. 7, 1125-28, 1997) 1 Tab. 15 Ref.

CODEN: TELEAY ISSN: 0040-4039

AVAIL. OF DOC.: Sepracor Inc., 111 Locke Dr., Marlborough, Massachusetts 01752, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The 4 stereoisomers of the bronchodilator formoterol (1) were prepared using asymmetric catalytic borane reductions with chiral oxazaborolidines as reducing agents. The procedure involved enantioselective synthesis of the intermediate epoxide (2), utilizing the previously developed enantioselective, cis-1-amino-2-indanol catalysed borane reduction. (R,R)-Formoterol was obtained in good chemical purity containing 2-3% of undesired diastereomer. Crystallization of (R,R)-**formoterol** with L-tartaric acid in **aqueous** isopropanol (85%) finally afforded the pure diastereomer. Likewise, (R,S)-, (S,R)- and (S,S)-formoterol-tartrates were obtained via the same synthetic sequence by reacting the appropriate epoxide with the appropriate amine.

CT [01] FORMOTEROL \*OC; FORMOTERO \*RN; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; OC \*FT; STEREOCHEM. \*FT; STEREOISOMER \*FT; STEREOSELECTIVE \*FT; SYMPATHOMIMETICS-BETA \*FT; SYNTH. \*FT

RN: 73573-87-2

L99 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:513756 CAPLUS

DOCUMENT NUMBER: 125:151185

TITLE: Pharmaceutical aerosols containing sugars and fluorocarbons or fluorochlorohydrocarbons

INVENTOR(S): Green, Alexander Peter

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9619968	A1	19960704	WO 1995-EP5085	19951222
W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,			

NE, SN, TD, TG

AU 9643469	A1	19960719	AU 1996-43469	19951222
EP 799024	A1	19971008	EP 1995-942192	19951222
EP 799024	B1	20000809		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV

JP 10511376	T2	19981104	JP 1995-520196	19951222
AT 195249	E	20000815	AT 1995-942192	19951222
ES 2150022	T3	20001116	ES 1995-942192	19951222
US 5955439	A	19990921	US 1997-849538	19970624

PRIORITY APPLN. INFO.: GB 1994-26252 A 19941224  
WO 1995-EP5085 W 19951222

AB Aerosol formulations for the administration of medicaments by inhalation comprises (a) particulate medicament; (b) at least one sugar; and (c) a fluorocarbon or hydrogen-contg. chlorofluorocarbon propellant. Particulate lactose was dispensed into clean, dry glass bottles and the metering valve was fitted onto the bottles, then micronized fluticasone propionate mixed with 1,1,1,2-tetrafluoroethane was pressure-filled into the canisters through the metering valve. The resultant inhalers delivered 25 .mu.g of fluticasone propionate/actuation.

CT Allergy inhibitors  
CT Inflammation inhibitors  
CT Soybean  
CT Surfactants  
CT Carbohydrates and Sugars, biological studies  
CT Lecithins  
CT Steroids, biological studies  
CT **Pharmaceutical dosage forms**  
CT Hydrocarbons, biological studies  
CT Hydrocarbons, biological studies

L99 ANSWER 38 OF 48 MEDLINE

ACCESSION NUMBER: 97060958 MEDLINE

DOCUMENT NUMBER: 97060958 PubMed ID: 8905004

TITLE: **Formoterol** inhaled as dry powder or via pressurized metered-dose inhaler in a cumulative dose-response study.

AUTHOR: Ullman A; Lofdahl C G; Melander B; Svedmyr N

CORPORATE SOURCE: Department of Clinical Pharmacology, Sahlgrenska Hospital, Goteborg, Sweden.

SOURCE: ALLERGY, (1996 Oct) 51 (10) 745-8.  
Journal code: 39C; 7804028. ISSN: 0105-4538.

PUB. COUNTRY: Denmark  
(CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970227  
Last Updated on STN: 19970227  
Entered Medline: 19970212

AB **Formoterol** administered by a dry-powder (DP) capsule inhaler was compared with a pressurized metered-dose inhaler (pMDI) with regard to bronchodilating and systemic effects. The study used a double-blind, crossover, double-dummy technique. Twelve patients with moderate reversible asthma in a stable phase were examined on two separate study days, and the inhalers were given in randomized order. After baseline measurements, increasing doses of **formoterol** were given at intervals of 75 min. FEV1 and heart rate and tremor measurements were



repeated after each dose, and the doses were 12 + 12 + 24 + 48 micrograms, giving a total dose of 96 micrograms. The peak expiratory flow rate (PEFR) was recorded in the morning before the first dose, after the last dose, and then repeatedly at home until 19 h after the last dose. There was an equal increase in ventilatory capacity at each dose level, independent of inhaler device. Repeated PEFR measurements after the last dose did not reveal any differences in duration of effect. There was a slight but statistically significant increase in heart rate and tremor after the highest doses of the DP formulation compared to the pMDI. These systemic effects can probably be explained by the reduced oral deposition of the aerosol caused by using a spacer. This study indicates that the DP and pMDI formulations of **formoterol** are equipotent in bronchodilation.

CT Check Tags: Comparative Study; Human; Male  
Administration, Inhalation  
Adult  
Aged  
\*Asthma: DT, drug therapy  
\*Bronchodilator Agents: AD, administration & dosage  
Capsules  
Cross-Over Studies  
Dose-Response Relationship, Drug  
Double-Blind Method  
\*Ethanolamines: AD, administration & dosage  
Middle Age  
\*Nebulizers and Vaporizers  
Peak Expiratory Flow Rate: DE, drug effects  
Powders  
Therapeutic Equivalency  
Time Factors

L99 ANSWER 39 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1996-11772 DRUGU P

TITLE: Pharmacological basis for duration of effect:  
**Formoterol** and salmeterol versus short-acting  
beta2-adrenoceptor agonists.

AUTHOR: Linden A; Rabe K F; Lofdahl C G

CORPORATE SOURCE: Univ.Göteborg

LOCATION: Göteborg, Swed.; Grosshansdorf, Ger.

SOURCE: Lung (174, No. 1, 1-22, 1996) 12 Fig. 1 Tab. 53 Ref.  
CODEN: LUNGD9 ISSN: 0341-2040

AVAIL. OF DOC.: Cardiovascular Research Institute Box 0130, University of  
California San Francisco, 505 Parnassus Avenue, San  
Francisco, California, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The pharmacology of long-acting versus short-acting beta-2 adrenoceptor agonists is reviewed, with reference to studies on animal and human airways in-vitro and in-vivo. The beta-2 agonists considered include the long-acting **formoterol** and salmeterol, and the short-acting isoprenaline and salbutamol, with clenbuterol as an intermediate case. Lipophilicity appears to be necessary but not sufficient in determining the bronchodilatory duration of action of these compounds, and receptor affinity, selectivity, potency and efficacy may also be involved. It is possible that specific exo-receptors (binding sites other than the adrenoceptor) exist for these compounds, but nonspecific partitioning into the cell membrane, followed by lateral diffusion, is also possible for the very lipophilic salmeterol.

CT IN-VITRO \*FT; HUMAN \*FT; LAB.ANIMAL \*FT; ANTIASTHMATIC \*FT; REVIEW \*FT  
[01] ANTIASTHMATICS \*FT; MAIN-TOPIC \*FT; PH \*FT  
[02] **FORMOTEROL** \*PH; SALBUTAMOL \*PH; SALMETEROL \*PH; ISOPRENALINE  
\*PH; PH \*FT

L99 ANSWER 40 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1995-23881 DRUGU P T

TITLE: Salmeterol.

AUTHOR: Johnson M

CORPORATE SOURCE: Glaxo

LOCATION: Uxbridge, U.K.

SOURCE: Med.Res.Rev. (15, No. 3, 225-57, 1995) 17 Fig. 8 Tab. 122

Ref.

CODEN: MRREDD ISSN: 0198-6325

AVAIL. OF DOC.: Glaxo Research and Development Ltd., Uxbridge, Middlesex,  
UB11 1BT, England.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Salmeterol is reviewed with reference to the molecule and its interaction with the beta-adrenoceptor, its pharmacology, including affinity and efficacy, involvement of intracellular mediators, onset and duration of action, enantiomers and beta-receptor desensitization. Bronchodilator and nonbronchodilator effects are also discussed. Finally clinical experience is presented. Representative beta-adrenoceptor agonists include adrenaline, isoprenaline, orciprenaline, terbutaline, salbutamol, pibuterol, fenoterol, clenbuterol, proctaerol, quinprenaline and **formoterol**.

CT REVIEW \*FT; STRUCT.ACT. \*FT; ADRENERGIC-RECEPTOR \*FT; BRONCHODILATOR  
\*FT; CLIN.TRIAL \*FT; RECEPTOR \*FT

[01] SALMETEROL \*TR; SALMETERO \*RN; MAIN-TOPIC \*FT; MODE-OF-ACT. \*FT;  
BRONCHODILATORS \*FT; ANTIASTHMATICS \*FT; SYMPATHOMIMETICS-BETA \*FT;  
89365-50-4 \*FT; TR \*FT; PH \*FT

RN: 89365-50-4

[02] ADRENALINE \*PH; ISOPRENALINE \*PH; ORCIPRENALINE \*PH; TERBUTALINE \*PH;  
SALBUTAMOL \*PH; PRIBUTEROL \*PH; FENOTEROL \*PH; CLENBUTEROL \*PH;  
PROCTAEROL \*PH; QUINPRENALINE \*PH; **FORMOTEROL** \*PH; PH \*FT

L99 ANSWER 41 OF 48 MEDLINE

ACCESSION NUMBER: 94174131 MEDLINE

DOCUMENT NUMBER: 94174131 PubMed ID: 7907426

TITLE: [The effect of a single dose of **formoterol** using  
an aerosol inhaler in asthmatic children. A randomized,  
controlled, double-blind study].

Effet d'une dose unique de **formoterol** par voie  
d'aerosol-doseur chez l'enfant asthmatique. Une etude  
randomisee, controllee, en double aveugle.

AUTHOR: Lebecque P; Vliers S; De Saint-Moulin T; Godding V

CORPORATE SOURCE: Pneumologie Pediatrique, Cliniques St-Luc, Universite  
Catholique de Louvain, Bruxelles, Belgique.

SOURCE: REVUE DES MALADIES RESPIRATOIRES, (1994) 11 (1) 47-50.  
Journal code: RZ9; 8408032. ISSN: 0761-8425.

PUB. COUNTRY: France

(CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199404

ENTRY DATE:           Entered STN: 19940420  
                  Last Updated on STN: 19970203  
                  Entered Medline: 19940414

AB   The duration of action of inhaled **formoterol**, a new long-acting beta-2-agonist, was compared to inhaled salbutamol and placebo in a double-blind, randomized, cross-over study in 16 children (8-12 years old) with stable moderate to severe asthma. Mean baseline FEV1 was 68 +/- 8% predicted. On the 4 study days, baseline FEV1 was within 15% of the FEV1 on visit 1. Two-three days apart, each patient inhaled either placebo, salbutamol (200 micrograms) **formoterol** (12 or 24 micrograms). FEV1 and PEF were measured repeatedly during 8 and 12 hours respectively. After **formoterol**, improvement over placebo remained significant at 8 hours for FEV1 ( $p = 0.006$ ) and 12 hours for PEF ( $p = 0.01$ ). When compared to salbutamol, it was significant at 8 hours for PEF ( $p = 0.03$ ). There were no significant differences in lung function when comparing the 12 micrograms and 24 micrograms doses of **formoterol**. Side-effects were minimal.

CT   Check Tags: Female; Human; Male  
      Adrenergic beta-Agonists: AD, administration & dosage  
      Adrenergic beta-Agonists: AE, adverse effects  
      \*Adrenergic beta-Agonists: TU, therapeutic use  
      **Aerosols**  
      Albuterol: AD, administration & dosage  
      Albuterol: AE, adverse effects  
      Albuterol: TU, therapeutic use  
      \*Asthma: DT, drug therapy  
      Bronchodilator Agents: AD, administration & dosage  
      Bronchodilator Agents: AE, adverse effects  
      \*Bronchodilator Agents: TU, therapeutic use  
      Child  
      Double-Blind Method  
      Drug Tolerance  
      Ethanalamines: AD, administration & dosage  
      Ethanalamines: AE, adverse effects  
      \*Ethanalamines: TU, therapeutic use  
      Forced Expiratory Volume: DE, drug effects  
      **Nebulizers and Vaporizers**  
      Peak Expiratory Flow Rate: DE, drug effects  
      Placebos  
      Time Factors

L99   ANSWER 42 OF 48   DRUGU   COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1993-30909   DRUGU   P

TITLE:           The Pharmacology of Salmeterol.

AUTHOR:           Johnson M; Butchers P R; Coleman R A; Nials A T; Strong P;  
                  Sumner M J

CORPORATE SOURCE: Glaxo

LOCATION:          Ware, United Kingdom

SOURCE:          Life Sci. (52, No. 26, 2131-43, 1993) 7 Fig. 4 Tab. 45 Ref.  
                  CODEN: LIFSAK           ISSN: 0024-3205

AVAIL. OF DOC.:   Department of Cardiovascular and Respiratory Pharmacology,  
                  Glaxo Group Research Ltd., Ware, Hertfordshire, England. (8  
                  authors).

LANGUAGE:         English

DOCUMENT TYPE:    Journal

FIELD AVAIL.:     AB; LA; CT

FILE SEGMENT:     Literature

AB   The pharmacology of salmeterol (SA) is reviewed. Other drugs discussed include salbutamol, isoprenaline, **formoterol**, propranolol and sotalol. Due to its potent and prolonged activation of beta-2

adrenoceptors in airway smooth muscle cells, endothelial cells, mast cells and epithelial cells, SA induces prolonged bronchodilatation, reduced vascular permeability, inhibition of inflammatory mediators, stimulation of ciliary function and modulation of ion and water transport across the bronchial mucosa. (congress).

CT HUMAN \*FT; GUINEA-PIG \*FT; IN-VITRO \*FT; AIRWAY \*FT; TRACHEA \*FT; LUNG \*FT; REVIEW \*FT; BRONCHODILATOR \*FT; RESPIRAT.TRACT \*FT; SYMPATHOMIMETIC-BETA \*FT; LAB.ANIMAL \*FT

[01] SALMETEROL \*PH; SALMETERO \*RN; MAIN-TOPIC \*FT; BRONCHODILATORS \*FT; ANTI-ASTHMATICS \*FT; SYMPATHOMIMETICS-BETA \*FT; PH \*FT

RN: 89365-50-4

[02] INFLAMMATION \*OC; SALBUTAMOL \*PH; ISOPRENALINE \*PH; **FORMOTEROL** \*PH; PROPRANOLOL \*PH; SOTALOL \*PH; FENOTEROL \*PH; ICI-118551 \*PH; KETOTIFEN \*PH; THEOPHYLLINE \*PH; CROMOLYN \*PH; SALMETEROL \*PH; ANTI-INFLAMMATORY \*FT; CYCLIC-AMP \*FT; HISTAMINE \*FT; LEUKOTRIENE-C \*FT; LEUKOTRIENE-D4 \*FT; PH \*FT

L99 ANSWER 43 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1994-09553 DRUGU P

TITLE: Comparative Biophysical Analysis of Interactions Between **Formoterol**, Salbutamol or Salmeterol and Lipid Membranes.

AUTHOR: Jackel K; John E; Anderson G P

CORPORATE SOURCE: CIBA-Geigy

LOCATION: Basle, Switzerland

SOURCE: Eur.Resp.J. (6, Suppl. 17, 383S, 1993) 1 Tab. 2 Ref.

AVAIL. OF DOC.: Physics and Asthma Departments, Ciba-Geigy AG, 4002 Basel, Switzerland.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB **Formoterol** and salmeterol, but not salbutamol partitioned into synthetic lipid membranes in an in-vitro study. Synthetic membranes were composed of palmityl oleoylphosphatidylcholine and dioleoylphosphatidylserine. The results raise the possibility that transitory retention of **formoterol** and salmeterol in the lipid plasmalemma bilayer may determine duration of action after inhalation in-vivo. The apparent discrepancy between the 30-fold higher membrane affinity (log K<sub>pmem</sub>) of salmeterol compared to **formoterol** and their similar clinical duration of action in humans remains to be explained. (congress abstract).

CT IN-VITRO \*FT; MEMBRANE \*FT; PERMEABILITY \*FT; MODE-OF-ACT. \*FT; BRONCHODILATOR \*FT; LIPOPHILICITY \*FT; PHYS.CHEM. \*FT; DRUG-COMPARISON \*FT; SUBCELL.STRUCT. \*FT

[01] SALBUTAMOL \*PH; SALBUTAMO \*RN; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; TOCOLYTICS \*FT; PH \*FT

RN: 18559-94-9

[02] SALMETEROL \*PH; SALMETERO \*RN; BRONCHODILATORS \*FT; ANTI-ASTHMATICS \*FT; SYMPATHOMIMETICS-BETA \*FT; PH \*FT

RN: 89365-50-4

[03] **FORMOTEROL** \*PH; FORMOTERO \*RN; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; PH \*FT

RN: 73573-87-2

L99 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:589788 CAPLUS

DOCUMENT NUMBER: 115:189788

TITLE: Hydrofluorocarbon propellants for pharmaceutical aerosols

INVENTOR(S): Steele, Gerald; Somani, Asit; Lim, Joseph Geok Paan  
 PATENT ASSIGNEE(S): Fisons PLC, UK  
 SOURCE: PCT Int. Appl., 18 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9111173	A1	19910808	WO 1991-GB133	19910130
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
IL 97065	A1	19940125	IL 1991-97065	19910128
CA 2074495	AA	19910803	CA 1991-2074495	19910130
ZA 9100696	A	19911030	ZA 1991-696	19910130
EP 513127	A1	19921119	EP 1991-903548	19910130
EP 513127	B1	19950719		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503523	T2	19930610	JP 1991-503797	19910130
JP 2858948	B2	19990217		
ES 2075956	T3	19951016	ES 1991-903548	19910130
PRIORITY APPLN. INFO.:			GB 1990-2351	A 19900202
			GB 1990-23655	A 19901031
			GB 1990-26476	A 19901205
			WO 1991-GB133	W 19910130

AB A pressurized aerosol compn. comprises a liquefied hydrofluorocarbon propellant contg. substantially no nonhydrofluorocarbon solvent having dispersed therein a medicament and a fluorinated surfactant. The propellants are substantially taste- and odor-free and have suitable vapor pressures for the administration of medicaments by inhalation, yet are environmentally safe and acceptable. Thus, a compn. contg. nedocromil Na 0.200, FC 431 (fluorinated acrylic polymer) 0.061, and CF<sub>3</sub>CFH<sub>2</sub> 11.979 g was filled into Al aerosol canister.

CT Bronchodilators  
 CT **Pharmaceutical dosage forms**  
 CT Hydrocarbons, biological studies

L99 ANSWER 45 OF 48 MEDLINE  
 ACCESSION NUMBER: 91243435 MEDLINE  
 DOCUMENT NUMBER: 91243435 PubMed ID: 2036817  
 TITLE: The effect of maximal doses of **formoterol** and salbutamol from a metered dose inhaler on pulse rates, ECG, and serum potassium concentrations.  
 AUTHOR: Maesen F P; Costongs R; Smeets J J; Brombacher P J; Zweers P G  
 CORPORATE SOURCE: Department of Respiratory Diseases, De Wever Hospital, Heerlen, The Netherlands.  
 SOURCE: CHEST, (1991 Jun) 99 (6) 1367-73.  
 Journal code: D1C; 0231335. ISSN: 0012-3692.  
 PUB. COUNTRY: United States  
 (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RANDOMIZED CONTROLLED TRIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199107  
 ENTRY DATE: Entered STN: 19910719  
 Last Updated on STN: 19970203

Entered Medline: 19910703

AB In a randomized, double-blind, crossover cumulative study, the individual maximal bronchodilator dosages for **formoterol** (F) and salbutamol (S) were assessed for their respective influence on ECG, pulse rate, and serum potassium levels in 13 patients with stable and reversible asthma. The following dosages were administered with an interval of 1 h: 12-24-48-(48)-(48) micrograms for F and 100-200-400-400-(400)-(400) micrograms for S. The study day was discontinued if pulse rate was above 140 beats min<sup>-1</sup>, a flattening of T wave on the ECG was recorded, or a maximal bronchodilation in FEV<sub>1</sub> was observed (above 110 percent of the predicted value or an increase in FEV<sub>1</sub> in the last two measurements below 5 percent). The maximal individual dose of F administered was 84 micrograms in six patients, 132 micrograms in three patients, 180 micrograms in three patients, and 228 micrograms in one patient. For S, the maximal individual dose was 400 micrograms in three patients, 2,200 micrograms in eight patients, 3,000 micrograms in one patient, and 3,800 micrograms in one patient. The mean maximal increase in FEV<sub>1</sub> was 36.0 percent after F and 35.1 percent after S. Pulse rate increased from 73 to 83 beats.min<sup>-1</sup> after F and from 75 to 84 beats.min<sup>-1</sup> after S (both statistically significant). No pulse rate above 140 beats.min<sup>-1</sup> was observed. In the high-therapeutic range (up to 36 micrograms of F and 6,090 micrograms of S), no changes in potassium level were observed. In still higher dosages, mean potassium level decreased from 4.16 to 3.78 mmol.L<sup>-1</sup> after F and from 4.02 to 3.88 mmol.L<sup>-1</sup> after S (not clinically relevant). The lowest individual potassium level recorded was 3.1 mmol.L<sup>-1</sup>. No clinically important changes in ECG were observed. In conclusion, very high doses of F and S administered from a metered dose inhaler proved to be safe for patients.

CT Check Tags: Comparative Study; Female; Human; Male

\*Albuterol: AD, administration & dosage

Albuterol: PD, pharmacology

Albuterol: TU, therapeutic use

Asthma: BL, blood

Asthma: DT, drug therapy

Asthma: PP, physiopathology

\*Bronchodilator Agents: AD, administration & dosage

Bronchodilator Agents: PD, pharmacology

Bronchodilator Agents: TU, therapeutic use

Double-Blind Method

\*Electrocardiography: DE, drug effects

\*Ethanolamines: AD, administration & dosage

Ethanolamines: PD, pharmacology

Ethanolamines: TU, therapeutic use

Forced Expiratory Volume: DE, drug effects

Middle Age

**\*Nebulizers and Vaporizers**

\*Potassium: BL, blood

Pulmonary Ventilation: DE, drug effects

\*Pulse: DE, drug effects

L99 ANSWER 46 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1991-29154 DRUGU T

TITLE: 'Fog'-Induced Bronchospasm and Neutrophil Chemotactic Activity: Effect of Inhaled **Formoterol**.

AUTHOR: Zanotti E; Crotti P; Moscato G; Patruno V; Dellabianca A; Rampulla C

LOCATION: Pavia, Italy

SOURCE: Am.Rev.Respir.Dis. (143, No. 4, Pt. 2, A650, 1991) 2 Tab.

CODEN: ARDSBL ISSN: 0003-0805

AVAIL. OF DOC.: Clinica del Lavoro Foundation, Centro Medico di Montescano,

Pavia, Italy.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

AB In a double-blind study, 12 asthmatics (fog responders) were randomized to receive a single inhaled dose of **formoterol** (F), salbutamol (S), or placebo (P). Fog challenge (inhalation of ultrasonically nebulized distilled **water**) was performed after dosing. Lung function and neutrophil chemotactic activity (NCA) were also assessed. Only F was effective in preventing 'fog'-induced bronchospasm and release of NCA 6 hr after administration. (congress abstract).

CT ASTHMA \*TR; PNEUMOPATHY \*TR; IN-VIVO \*FT; CASES \*FT; DOUBLE \*FT; BLIND-TEST \*FT; PLACEBO \*FT; RANDOM \*FT; INHALATION \*FT; CLIN.TRIAL \*FT; ANTI-ASTHMATIC \*FT; LUNG \*FT; FUNCTION \*FT; RESPIRATION \*FT; DRUG-COMPARISON \*FT; BRONCHODILATOR \*FT; NEUTROPHIL \*FT; CHEMOTAXIS \*FT; LEUKOCYTE \*FT

[01] **FORMOTEROL** \*TR; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; FORMOTERO \*RN; TR \*FT

RN: 73573-87-2

[02] **SALBUTAMOL** \*TR; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; TOCOLYTICS \*FT; **SALBUTAMO** \*RN; TR \*FT

RN: 18559-94-9

L99 ANSWER 47 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1991-15484 DRUGU P T

TITLE: Effect of Inhaled **Formoterol** on 'Fog'-Induced Bronchospasm: A Double-Blind, Three-Period Cross-Over Study.

AUTHOR: Zanotti E; Crotti P; Moscato G; Dellabianca A; Rampulla C

LOCATION: Pavia, Italy

SOURCE: Eur.Resp.J. (3, Suppl. 10, 133S-134S, 1990) ISSN: 0903-1936

AVAIL. OF DOC.: Clinica del Lavoro Foundation, Montescano, Pavia, Italy.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The efficacy and tolerability of single inhaled doses of **formoterol** (F), salbutamol (S) and placebo (P) in preventing ultrasonically nebulized distilled **water** (i.e. 'fog')-induced bronchospasm were compared in 12 asthmatic patients enrolled in a double-blind, within-patient, 3-period crossover study. It was found that only F was still effective in protecting against fog-induced asthma 6 hr after administration. (congress abstract).

CT ASTHMA \*TR; PNEUMOPATHY \*TR; BRONCHOSPASM \*OC; PNEUMOPATHY \*OC; **WATER** \*RC; CASES \*FT; IN-VIVO \*FT; DRUG-COMPARISON \*FT; PLACEBO \*FT; DOUBLE \*FT; BLIND-TEST \*FT; CROSSOVER \*FT; PROPHYLAXIS \*FT; INDUCED \*FT; ANTI-ASTHMATIC \*FT

[01] **FORMOTEROL** \*PH; **FORMOTEROL** \*TR; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; FORMOTERO \*RN; PH \*FT; TR \*FT

[02] **SALBUTAMOL** \*PH; **SALBUTAMOL** \*TR; ANTI-ASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS-BETA \*FT; TOCOLYTICS \*FT; **SALBUTAMO** \*RN; PH \*FT; TR \*FT

L99 ANSWER 48 OF 48 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1984-08645 DRUGU P A

TITLE: The Development of a Radioimmunoassay for **Formoterol**

AUTHOR: Yokoi K; Murase K; Shiobara Y

CORPORATE SOURCE: Yamanouchi  
LOCATION: Tokyo, Japan  
SOURCE: Life Sci. (33, No. 17, 1665-72, 1983) 7 Fig. 8 Ref.  
CODEN: LIFSAK ISSN: 0024-3205  
AVAIL. OF DOC.: Institute of Research and Development, Yamanouchi  
Pharmaceutical Co. Ltd., Azusawa 1-1-8, Itabashi-ku, Tokyo,  
Japan.  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT; MPC  
FILE SEGMENT: Literature  
AB An RIA for **formoterol** was developed. Its sensitivity was 0.1  
ng/ml in plasma and urine and cross reactivity with glucuronide was 30%.  
Results compared favorably with those obtained by GS-MS. Plasma and  
urine **formoterol** levels were determined following p.o.  
administration of the fumarate to dogs and humans.  
[01] **FORMOTEROL** \*DM; **FORMOTEROL** \*OC; FUMARATE \*DM;  
FUMARATE \*OC; P.O. \*FT; DOG \*FT; HUMAN \*FT; URINE \*FT; CONC. \*FT;  
RADIOIMMUNODET. \*FT; QUANT. \*FT; DET. \*FT; BLOOD-PLASMA \*FT;  
ANTIASTHMATICS \*FT; BRONCHODILATORS \*FT; SYMPATHOMIMETICS \*FT;  
LAB.ANIMAL \*FT; ANALYSIS \*FT; SEROLOGY \*FT; FORMOTERO \*RN; DM \*FT; OC  
\*FT